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Remarks:

•The applicant has subsequently filed a sequence listing and declared, that it includes no new matter. •Claims 11 to 12 are deemed to be abandoned due to non-payment of the claims fees (Rule 31 (2) EPC).

(54) Gastric helicobacter 16 S rDNA sequences from cattle and pigs and their use for detection and typing of Helicobacter strains

(57) The present invention relates to new Helicobacter 16S rRNA or rDNA polynucleotide sequenceuseful for detection and typing of Helicobacter infacted human and animal samples. The present invention relates more particularly to new "Candidatus Helicobacter bovis" and "Candidatus Helicobacter suis" sequences as defined in SEO ID NO 1 and 2, sequence variants and fragments thereof. These new Helicobacter sequences allow the design of sequence specific probes and primers for detection and typing of the strains they are derived from Degnostic methods and kits employing such new bovine and porcine Helicobacter sequences are also disclosed.

Description

[0001] The present invention relates to the field of detection and typing of *Helicobacter* infection in clinical samples from humans and other mammals. The present invention relates more particularly to bovine and porcine 16 rDNA polynucleotide sequences as well as their use in diagnostic applications.

[0002] In the 19th century, gastric spiral organisms were described for the first time in different animals (Rappin, 1881; Bizzozero, 1893; Salomon, 1896), Salomon observed spiral organisms in the stomachs of dogs, cats and the brown Norwegian rat but not in humans, monkeys, pigs, mice, pigeons, crows and cattle (Salomon, 1896). It was only in 1984 that a renewed interest emerged for similar organisms after the isolation of Helicobacter pylori from the human stornach (Marshall & Warren, 1984). The association of H. pylori with chronic gastritis, peptic ulceration and gastric cancer (Cover & Blaser, 1992; Blaser et al., 1991; Parsonnet et al., 1991) resulted in intensive research worldwide. Various Helicobacter species were isolated from the gastrointestinal tract of different animals. To date, the genus Helicobacter consists of 18 different species (On. 1996; Franklin et al., 1996; Mendes et al., 1996; Jalava et al., 1997; Trivett-Moore et al., 1997; Shen et al., 1997) and constitutes together with the genera Wolinella, Campylobacter and Arcobacter, the epsilon subdivision of the Proteobacteria, also known as rRNA superfamily VI (Vandamme et al., 1991). [0003] In 1992, two different groups almost simultaneously reported the presence of helically shaped bacteria in the abomasum of calves and adult cattle based on histological data (Günther & Schulze, 1992; Haringsma & Mouwen, 1992). Both groups described large numbers of spiral-shaped bacteria in the gastric crypts of the pyloric region and considered them as putative Helicobacter species. Further indirect evidence of the presence of Helicobacter-like organisms in adult cattle and calves was given by serological studies. Seidel et al. (1996) found significant titers of antibodies against H. pylori epitopes in the serum of calves after absorption with Campylobucter jejuni, Wolinella succinogenes, Escherichia coli and Proteus mirabilis strains. One report described a bactericidal activity of bovine serum, colostrum and milk against H. pylori (Korhonen et al., 1995). In vitro isolation of these organisms has not been successful so far (Jelinski et al., 1995; Braun et al., 1997) and the taxonomic status of these putative Helicobacter-like bacteria is unknown.

[0004] The pathogenic role of *H. pylori* lied to speculations about the association of bovine *Helicobacter-like* bacteria with abomasal ulcer disease, although no conclusive evidence has been provided to date (Günther & Schulze, 1992; Haringsrea & Mouwen, 1992). Other bacteria such as *Campylobacter* species and *Clostridium perifringers* have also been studied in association with the occurrence of abomasal lesions (Al Mashat & Taylor, 1980; Mills et al., 1990, Jelinski et al., 1995).

[0005] Within the 'genus 'Helicobacter, a phylogenetic subgroup of morphologically similar bacteria can be distinguished. These bacteria, characterized by their long and tightly coiled (gastrospirillum-like) appearance, have been observed in gastric biopsies of humans, cats, lemurs, dogs, pigs and exotic carnivores (Dent et al., 1987; Lee et al., 1988; Cribourke et al., 1992; Hanninen et al., 1998; Jalava et al., 1999; Oueliou et al., 1999; Deton et al., 1993, Jakob et al., 1997). Three species with this morphology (H. felis, H. bizozaeroni, H. selomonis) have been isolated and characterised from gastric samples of cats and dogs (Paster et al., 1991; Hänninen et al., 1996; Jalava et al., 1997). [0006] The observation of gistrospirillum-like organisms in humans was described for the first time in 1987 both et al (Dent et al., 1997). Although initially referred to as 'Castrospirillum-hominis' (McNutly et al., 1999), libis organism was later renamed "Helicobacter heilmanni" as 165 rDNA sequence analysis revealed that these human gastrospirilla belonged to the genus Helicobacter (O'Flourike et al., 1992; Sohick et al., 1993). From these results, it also became clear that there were at least two different types of "Helicobacter heilmanni", referred to as type 1 and type 2. This observation was based on a 3.5% sequence difference, suggesting that the two sequences represented two different species. The first isolation of a "Helicobacter heilmanni" - like bacterium from humans was recently reported by Andersen et al. (1996).

5 (0007] In pigs, pastrospiritum-like beateria were observed in the antral pits and at the mucosal surface of the stomach Cluienz et al., 1990) and have provisionally been named 'Gastrospiritum suit', (Mendes et al., 1990). Histopathological studies associated this bacterium with pyloric lymphonodular gastritis (Mendes et al., 1991) and gastric ulcer disease of the pars esceptings in pigs (Bartosae et al., 1995, Culercz et al., 1996). Although in vitro cutitivation of 'Gastrospirillum suis' has been unsuccessful (Queiror et al., 1995, in vivo-cutilivation in mico and ratis has been reported (Mourous et al., 1993, Mendes et al., 1996). In one case, a Helicobacter was isolated from the faceces of swine (Saymour et al., 1994) which was later characterised as Helicobacter purintensity (Devit et al., 1994). Then rembres of ITAM superfamily VI. Campylobacter hybrintestimalis subep. Lawsonii (On et al., 1995). Arcobacter butzleri and Arcobacter creaerophilus (Slavez et al., 1997), have also been isolated from the stomach of swine.

[0008] As "Gastrospirillum suis" remains unculturable, an official species designation is impossible according to the guidelines of the International Code of Nomenclature of Bactoria which are stating the necessity of a broad range of phenotypic and phylogenetic data. Murray and Schleifer (1994) anticipated this problem, and proposed a provisional status to record the properties of putative taxe of prokaryotes. This proposal was implemented in 1995 by the International Committee on Systematic Bacterioloxy by the Introduction of the provisional status Candidatus for the describtion

of uncultivable organisms based upon genomic data and to a certain extent structural, metabolic, reproductive and environmental characteristics (Murray and Stackebrandt, 1995).

[0009] It is an aim of the present invention to provide new Helicobacter nucleotide sequences of the 16S rRNA coding

[0010] It is also an aim of the present invention to provide new probes and primers for detection of Helicobacter species

[0011] It is also an aim of the present invention to provide methods and kits for detection and/or typing of Helicobacter species present in cattle and pigs.

[0012] It is further an aim of the present invention to provide methods and kits for detection of zoonoses in human samples.

[0013] It is also an aim of the present invention to provide new nucleotide sequences for studying and detecting the

occurrence of pathogenic Helicobacter strains in mammals, more particularly in cattle and pigs. [0014] All the aims of the present invention are met by the following embodiments.

[0015] According to one embodiment, the present invention relates to an isolated 16S rDNA Helicobacter polynucleic acid sequence selected from any of the following

(a) a sequence represented in any of SEQID NO 1 or 2, or the RNA version thereof,

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(b) a sequence which hybridizes under stringent conditions to any of the sequences set out in (a).

[0016] The term "16S ribosomal polynucleic acid sequences" as used in the present invention refers to 16S rRNA or 16S rDNA polynucleic acid sequences.

[0017] According to a first aspect of the present invention, seven abomasal biopsies of adult cattle were sampled from different Belgian and Dutch farms. In all samples the presence of Helicobacter-like organisms was demonstrated by biochemical, immunohistochemical and electronmicroscopical data, Bacterial 16S rDNA was amplified from each sample by PCR and sequences were determined either by direct or indirect sequence analysis. Pairwise comparisons revealed all sequences to be more than 99 % homologous. Phylogenetic analysis placed the organism, corresponding to the reference sequence R2XA, within the genus Helicobacter. Adiagnostic PCR-assay was designed, differentiating the bovine 16S rDNA sequences from those of 15 different Helicobacter strains and Wolinella succinogenes. These results indicated the corresponding organism to represent a single taxon. The low similarity level towards H. bilis (92.8 %), its closest validly named neighbour, strongly suggests that this novel taxon indeed is a novel Helicobacter species. An in situ hybridisation procedure associated the bovine sequences to the Helicobacter-like organisms in the abomas-

[0018] According to a second aspect, the present invention relates to new Helicobacter sequences from pigs. Stomachs of five slaughterhouse pigs originating from different Belgian and Dutch farms were selected based on the presence of "Gastrospirillum suis"-like bacteria as demonstrated by biochemical, immunohistochemical and electronmicroscopical data. Using broad range primers, bacterial 16S rDNA was amplified by PCR and five Helicobacter-like sequences were determined either by direct or indirect sequence analysis. An intersequence homology of 99,7 % was observed, suggesting that the sequences originated from strains belonging to a single species. Phylogenetic analysis of the consensus sequence placed the organism within the genus Helicobacter, where it formed a distinct subgroup together with other gastrospirillum-like bacteria (H. felis, H. bizzozeronii, H. salomonis, "H heilmannii" type 1 and type 2). Diagnostic PCR primers and a probe were developed, differentiating the porcine sequences from all known Helicobacters. These results indicate that the porcine sequences represent a single taxon within the genus Helicobacter. The low similarity level towards H. salomonis (96.6 %), its closest validly named neighbour, strongly suggests that this novel taxon indeed is a novel Helicobacter species. In situ hybridisation experiments linked the reference sequence to the "Gastrospirillum suis"-like bacteria. On the basis of these results, the name "Candidatus Helicobacter suis" for

this new gastric Helicobacter from pigs is proposed. [0019] These sequences are commonly characterized by the fact that they can be used to study and most probably detect pathogenic Helicobacter strains in mammats, more particularly in cattle and pigs. Such pathogenic strains cause for instance gastric ulcers and chronic gastritis.

[0020] The present invention relates more particularly to an isolated polynucleic acid sequence as defined above represented by any of SEQ ID NO 1 or 2 or 15 to 24.

[0021] The present invention also relates to an isolated polynluceic acid sequence as defined above which is more than 92.8%, preferably more than 93.5%, more preferably more than 95% and most preferably more than 97.5% homologous to SEQ ID NO 1. Other preferred ranges of homology include 93, 94, 94.5, 95.5, 96, 96.5, 97, 98, 98.5, 99

[0022] Sequences which have a homology of more than 92.8% to SEQ ID NO 1 are considered to belong to the same group of organisms as the one where SEQ ID NO 1 has been derived from.

- [0023] According to the present invention, the homologies of SEQ ID NO 1 were calculated by means of the GE-NESCAN program (Applied Maths byba, Risquons-toutstraat 38, B-8511 Kortrijk, Belgium).
- [0024] The term "homology" refers to a sequence identity as calculated by the above-given program.
- [0025] SEQ ID NO 2 is 99.5% homologous to the closest found sequence. Sequences of more than 99.5% homology compared to SEQ ID NO 2 are also within the scope of the present invention.
- [0026] Preferred sequences according to the present invention are set out in Figures 1, 2, 4 and 5: SEQ ID NO 1 to 2 and 15 to 24. Also unique parts and fragments of these sequences are part of the present invention. Preferred unique parts are set out in Table 2.
- [0027] Since SEQ ID NO 2 shows 96.6% homology to its closest found validly named neighbour, the use of sequences of more than 96.6% homology to SEQ ID NO 1 for identification or typing of Helicobacter species is also within the scope of the present invention. Preferably sequences of more than 97%, 97.5%, 98%, 98.5%, 99% or 99.5% homology to SEQ ID NO 2 are used for this goal.
- [0028] According to another embodiment, the present invention relates to a part of an isolated polynucleic acid as defined above, more particularly part or a fragment of SEQ ID NO 1 or 2, wherein said part is unique to the polynucleic acid sequence it is derived from.
- [0029] According to the present invention, the term "unique" implies that at least one nucleotide of the fragment or part is different from a nucleotide present at the same nucleotide position in a known 16S rRNA sequence or the corresponding gene. Such a nucleotide can be deduced theoretically by looking at an alignment of the new sequences of this invention with other closely related Helicobacter 16S rDNA gene nucleotide sequences (see Figures 1, 2, 4 and
- 5). Said type of nucleotides are unique to the sequence they are derived from. These fragments are thus not part of any known 16S rRNA or gene sequence encoding the same. The fragments according to this embodiment of the present invention may be of any length between 10 to the maximum number of nucleotides of SEQ ID NO 1 or 2 or its variants. Preferred lengths are 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, etc. nucleotides.
- [0030] According to another embodiment, the present invention relates to a probe which specifically hybridizes to a polynucleic acid sequence as defined above.
 - [0031] Preferred probes are given in Table 2. Probe R628f is a preferred "Candidatus Helicobacter bovis" specific probe, Probe V100f is a preferred "Candidatus Helicobacter suis" specific probe. Other suitable probes may be derived from a visual inspection of the alignment shown in Figure 1 or 2.
 - [0032] According to another embodiment, the present invention relates to a primer which specifically amplifies a polynucleic acid sequence as defined above.
 - [0033] Preferred primers according to the present invention are given in Table 2. Primers R5741 and R832r are preferred "Candidatus Helicobacter bovis" specific primers and are suited for a specific PCR and in situ hybridisation assays. Primers VB32f and V1621r are preferred *Candidatus Helicobacter suis* specific primers for a specific PCR and in situ hybridisation assays. Other suitable primers according to the present invention may be derived from a visual inspection of the alignment shown in Figure 1 or 2.
 - [0034] Relying on the principles well kown in the art, the skilled man will be able to select primers that allow specific amplification of SEQ ID NO 1 or 2 or the claimed variants thereof under given or experimental conditions, such as temperature, buffer composition, polymerase chain reaction cycle etc. Likewise the skilled man will be able to select probes that specifically hybridize to either SEQ ID NO 1 or 2 or the claimed variants under given experimental conditions such as temperature, buffer composition etc. Having chosen primers and/or probes, the skilled man will furthermore be able to assess the efficacy of these primers or probes without undue experimentation. It is also obvious that the skilled man may chose to combine more than one primer pair or more than one probe to carry out the method defined above
- [0035] In some cases, one may not wish to detect all SEQ ID NO 1 or 2 variants as specified above, for instance if one intends to detect alleles found in a certain geographic region.
 - [0036] According to another embodiment, the present invention relates to a method for detection and/or typing of Helicobacter strains present in a biological sample comprising hybridizing the 16S rRNA or 16S rDNA target region polynucleotides of said Helicobacter strains present in said biological sample with at least one probe as defined above. [0037] Preferably said method may be used to study and detect the occurrence of pathogenic Helicobacter strains.
- [0038] According to another embodiment, the present invention relates to a method for detection and/or typing of Helicobacter strains present in a biological sample comprising specifically amplifying the 16S rRNA or 16S rDNA target region polynucleotides of said Helicobacter strains present in said biological sample with at least one primer as defined above.
- [0039] Preferably said method may be used to study and detect the occurrence of pathogenic Helicobacter strains. [0040] A preferred embodiment according to the present invention involves a method for detection and/or typing of Helicobacter strains present in a biological sample comprising first amplifying a specific target region encompassed in or comprising the 16S rRNA region of said Helicobacter strains present in said biological sample and subsequently hybridizing the 16S rRNA or 16S rDNA target region polynucleotides of said Helicobacter strains present in said bio-

logical sample with at least one (or more than one) probe as defined above.

[0041] Different techniques can be applied to perform the methods of the present invention. These techniques may comprise immobilizing the target polymucleic acids, possibly after amplification, on a solid support and performing a hybridization with labelled oligonucleotide probes of the present invention. Alternatively, said probes may be immobilized on a solid support and hybridization may be performed with labelled target polynucleic acids, possibly after am-

plification (i.e. a reverse hybridization).

[0042] A preferred method according to the present invention is an instituty/ordisation assay (see Examples section). [0043] The well-known technique of Southern blotting is one example of a hybridization assey that can be used to perform the methods of the present invention. Another example of a hybridization technique is the DNA enzyme immuno assay (DEIA). According to this method. PCR products are generated by a primer set, of which either the forward or the reverse primer contain bottom at the 5' end. This allows binding of the biothylated amplimers to streptavidin-coated microtiter wells. PCR products are denatured by sodium hydroxide, which allows removal of the non-biothylated strand. Specific digoxigation (DIG) sibelled origonucleotide probes are hybridized to the single-stranded immobilized PCR product.

uct and hybrids are detected by enzyme-labelled conjugate and colorimetric methods.

[0044] A Convenient reverse hybridization technique is the LPAP assay. The LPAP uses oligonucleotide probes immobilized as parallel lines on a solid support strip (Stuyver et al. 1993; International patent application WO 94/12670).

This approach is particularly advantageous since it is fast and simple to perforce, in particularly advantageous since it is fast and simple to perform.

[0045] It is to be understood that any other type of hybridization assay or hybridization format using any of the selected probes as described further in the invention, is also covered by the present invention.

[0046] According to another embodiment, the present invention relates to a diagnostic kit for detection and/or typing of Helicobacter strains comprising:

- at least one probe as defined above and/or,
- at least one primer as defined above.

[0047] According to another embodiment, the present invention relates to a medicament comprising a polynucleic acid sequence as defined above.

[0048] According to another embodiment, the present invention relates to a polynucleic acid sequence as defined above for use as a medicament.

[0049] The following definitions and explanations will permit a better understanding of the present invention.

[0050] The target marierial in the samples to be analysed may either be DNA or RNA e.g. genomic DNA messaches RNA, viral RNA or RNA e.g. genomic DNA messaches RNA, viral RNA or RNA or a political versions thereof. These molecules are in this application also temend "polynucles acide" or RNA or PNA or a political version before or RNA or DNA or a political version before or RNA or DNA or a political version before or RNA or DNA or a political version before or RNA or DNA or a political version before or RNA or DNA or a political version before or RNA or DNA or a political version before or RNA or DNA or a political version before or RNA or DNA or a political version before or RNA or DNA or a political version before or RNA or RNA or a political version before the political version before t

[0051] Well-known extraction and purification procedures are available for the isolation of RNA or DNA from a sample (e.g. in Sambrook et al. 1989).

[0052] The term "probe" according to the present invention refers to a single-stranded oligonucleotide which is designed to specifically hybridize to "Candidatus Helicobacter bovis or suis" polynucleic acids.

[0053] The term 'primer' refers to a single stranded oligonucleotide sequence capable of acting as a point of initiation for synthesis of a primer extension product which is complementary to the nucleic acid strand to be copied. The length and the sequence of the primer must be such that they allow toprime the synthesis of the extension products. Preferably the primer is about 5-50 nucleotides long. Specific length and sequence will depend on the complexity of the required DNA or RNA targets, as well as on the conditions at which the primer is used, such as temperature and onic strength. It is to be understood that the primers of the present invention may be used as probes and vice versa, provided that the experimental conditions are adapted.

[0054] The expression "suitable primer pair" in this invention refers to a pair of primers allowing specific amplification of a "Candidatus Helicobacter bovis or suis" polynucleic acid fragment.

[0055] The term 'target region' of a probe or a primer according to the present invention is a sequence within the 'Candidatus Helicobacter bovis or suis' polynucleic acids to which the probe or the primer is completely complementary or partially complementary (i.e. with some degree of mismatch). It is to be understood that the complement of said target sequence is also a suitable target sequence in some cases.

[0056] "Specific hybridization" of a probe to a target region of respectively the "Candidates Helicobacter bovis" polynucleia calcib means that said probe forms a duplex with part of this region or with the entire region under the experimental conditions used, and that under those conditions said probe does not form a duplex with other regions of the polynucleia calcib present in the sample to be analysed.

[0057] "Specific hybridization" of a primer to a target region of respectively the "Candidatus Helicobacter bovis" or "Candidatus Helicobacter suis" polynucleic acids means that, during the amplification step, said primer forms a duplex

with part of this region or with the entire region under the experimental conditions used, and that under those conditions said primer does not form a duplex. With other regions of the polynucles acids present in the sample to be analysed. It is to be understood that "duplex" as used hereby, means a duplex that will lead to specific amplification.

[0058] "Specific amplification" of a fragment of respectively the "Candidatus Helicobacter bovis" or Candidatus Helicobacter sus* polyuneties acids means amplification of the fragment for which the primers were designed, and not of any other fragment of the polyuncials acids present in a sample.

[0059] The fact that amplification primers do not have to match exactly with the corresponding target sequence in the template to warrant proper amplification is amply documented in the literature (Kwok et al., 1990). However, when the primers are not completely complementary to their target sequence, it should be taken into account that the amplified fragments will have the sequence of the primers and not of the target sequence. Primers may be labelled with a label of choice (e.g. biotine). The amplification method used can be either polymerase chain reaction (CRP, Saliti et al., 1988), ligase chain reaction (LCRP, Landgren et al., 1988; Wu & Wallace, 1989; Barany, 1991), nucleic acid sequence-based amplification (NASBA, Guatelli et al., 1990; Compton, 1991), transcription-based amplification system (TAS; Kwot et al., 1989), strand displacement amplification (SDAP Duck 1990) or amplification by means of OS replicases

(Lomei et al., 1969) or any other suitable method to amplify nucleic acid molecules known in the art. [0060] Preferably, the probes of the invention are about 5 to 50 nucleotides long, more preferably from about 10 to 25 nucleotides long, more preferably from about 10 to 25 nucleotides. Particularly preferred lengths of probes include 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 or 25 nucleotides. The nucleotides as used in the present invention may be ribonucleotides, decoyribonucleotides and modified nucleotides such as inosine or nucleotides containing modified groups which do not essentially alter their hybridization characteristics.

[0061] Probe and primer sequences are represented throughout the specification as single stranded DNA oligonucleotides from the 5" to the 3" end. It is obvious to the man skilled in the art that any of the below-specified probes can be used as such, or in their comolementary form, or in their RNA form (wherein Ts is reduced by U).

[0062] The probes according to the invention can be prepared by cloning of recombinant plasmids containing inserts sincluding the corresponding nucleotide sequences, if need be by excision of the latter from the cloned plasmids by use of the adequate nucleases and recovering them, e.g. by fractionation according to molecular weight. The probes according to the present invention can also be synthesized chemically, for instance by the conventional phospho-triester method.

[0063] The oligonucleotides used as primers or probes may also comprise nucleotide analogues such as phosphorothiates (Miler et al., 1979) or peptide nucleic acids (Nielsen et al., 1993). The state of the contract of the c

[0064] The term "solid support" can refer to any substrate to which an oligonucleotide probe can be coupled, provided that it retains its hybridization renaise and provided that it teatine its hybridization renaise and provided that the background level of hybridization renaise low. "Usually the solid substrate will be a microtiter plate, a membrane (e.g., nylon or nitrocellulose) or a microsphere (bead) or a chip. Prior to application to the membrane or fixation it may be convenient to modify the nucleic acid probe in order to facilitate fixation or improve the hybridization efficiency. Such modifications may encompass homopolymer tailing, coupling with different reactive groups such as aliphatic groups, NH₂ groups, SH groups, carboxylic groups, or coupling with bidin, haptens or proteins.

45 [0065] The term "labelled" refers to the use of labelled nucleic acids. Labelling may be carried out by the use of labelled nucleotides incorporated during the polymerase step of the amplification such as illustrated by Saiki et al. (1999) or labelled primers, or by any other method known to the person skilled in the art. The nature of the label may be isotopic (42P, 35S, etc.) or non-isotopic (blotin, digoxigenin, etc.).

[0066] The "biological sample" may be for instance cultured *Helicobeacter* strains, gastric, abomasal stomachs, crassal stomachs, reticulum and rumen, or duodenal biopaise (fresh or parafine material), faeces, saliva, mouth mucosa, gastric juice or urine. Preferably these samples may be taken from piglets, pigs, humans, calves, cattle, etc.

[0067] For designing probes with desired characteristics, the following useful guidelines known to the person skilled in the art can be applied.

[0068] Because the extent and specificity of hybridization reactions such as those described herein are affected by a number of factors, manipulation of one or more of those factors will determine the exact sensitivity and specificity of a particular probe, whether perfectly complementary to its target or not. The importance and effect of various assay conditions are exclaimed further herein.

[0069] **The stability of the [probe : target] nucleic acid hybrid should be chosen to be compatible with the assay

conditions. This may be accomplished by avoiding long AT-rich sequences, by terminating the hybrids with G.C base pairs, and by designing the probe with an appropriate Tim. The beginning and and points of the probe should be chosen so that the length and %GC result in a Tim about 2-10EC higher than the temperature at which the final assay will be performed. The base composition of the probe is significant because G-C base pairs exhibit greater thermal stability as compared to A-T base pairs due to additional hydrogen bonding. Thus, hybridization involving complementary nucitic acids of higher G-C content will be more stable at higher temperatures.

[0070] **Conditions such as ionic strength and incubation temperature under which a probe will be used should also be taken into account when designing a probe. It is known that the degree of hybridization will increase as the ionic strength of the reaction mixture increases, and that the thermal stability of the hybridis will increase with increasing ionic strength. On the other hand, chemical reagents, even as stremamics, urea, DMSO and actionis, which disrupt hydrogen bonds, will increase the stringency of hybridization. Destabilization of the hydrogen bonds by such reagents can greatly reduce the Tim. In general, optimal hybridization for synthetic oligonucledide probes of about 10-50 bases in length occurs approximately SEC below the melling temperature for a given duplex incubation at temperatures below the optimum may allow mismatched base sequences to hybridize and can therefore result in reduced specificity. [0071] **It is desirable to have probes which hybridize only under conditions of high stringency. Under high stringency conditions only highly complementary nucleic acid hybrids will form, hybrids without a sufficient degree of complementarity will not form, Accordinol, the stringency of the assay conditions determines the amount of complementary for the sast or conditions of the service and the service of complementary will not form. Accordinol, the stringency of the assay conditions determines the amount of complementary will not form.

needed between two nucleic acid strands forming a hybrid. The degree of stringency is chosen such as to maximize

the difference in stability between the hybrid formed with the target and the non-target nucleic acid.

[0072] **Plegions in the target DNA or RNA which are known to form strong internal structures inhibitory to hybridization are less preferred. Likewise, probes with extensive self-complementarity should be avoided. As explained above, hybridization is the association of two single strands of complementary nucleic acids to form a hydrogen bonded double strand. It is implicit that if one of the two strands is wholly or partially involved in a hybrid hat it will be less able to participate in formation of a new hybrid. There can be intramolecular and intermolecular hybrids formed within the molecules of one type of probe if there is sufficient self complementarity. Such structures can be avoided through careful probe design. By designing a probe so that a substantial portion of the sequence of interest is single stranded, the rate and extend of hybridization may be greatly increased. Computer programs are available to search for this type of interaction. However, in certain instances, it may not be ossible to sould the type of interaction.

[0073] **Standard hybridization and wash conditions are disclosed in the Examples section. Other conditions are for instance 3X SSC (Sodium Saline Ottrae), 20% deionized FA (Formamich) at 15CC. Other solutions (SSPE (Sodium Saline phosphate EDTA), TMAC (Tetramethyl ammonium Chloride), etc.) and temperatures can also be used provided that the specificity and sensitivity of the probes in length or in sequence have to be carried out to maintain the specificity and sensitivity required under the given circumstances. [0074] The term "hybridization buffer" means a buffer allowing a hybridization reaction between the probes and the polynucleia acids present in the sample, or the amplified products, under the appropriate stringency conditions.

[0075] The term "wash solution" means a solution enabling washing of the hybrids formed under the appropriate stringency conditions.

(0076) The Examples as set out below only serve to illustrate the present invention. The contents of all references

FIGURE AND TABLE LEGENDS

referred to in this text are hereby incorporated by reference.

[0077]

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Figure 1 represents an alignment of the reference sequence FIZXA of "Candidatus Helicobacter bovis" (SEQ ID NO 1) with sequences of strains belonging to the spision subdivision (Table 3) which were retrieved from the EMBL data library and were aligned with reference sequence RZXA

Figure 2 represents an alignment of the reference sequence V2BXA of *Candidatus Helicobacter suis* (SEQ ID NO 2) sequence with the sequences of strains belonging to the same phylogenetic lineage (Table 3).

Figure 3A represents a phylogenetic tree based on the phylogenetic analysis of "Candidates Helicobacter bovis" as set out in the Examples section. The scale bar represents a one % difference in nucleotide sequences as determined by measuring the length of horizontal lines connection any two species.

Figure 3B represents a a phylogenetic tree based on the phylogenetic analysis of *Candidatus Helicobacter suis* as set out in the Examples section. The scale bar represents a one % difference in nucleotide sequences as determined by measuring the length of horizontal lines connecting any two species.

Figure 4 represents an alignment of the different 'Candidatus Helicobactor boxis' sequences. The reference sequences is PRASON (SECI D NO 1). The other sequences are RSEXON (SECI D NO 15), RSAXON (SECI D NO 17), The other sequences are RSEXON (SECI D NO 15), RSAXON (SECI D NO 17), R130001INV (SEQ ID NO 18), R27TOTAAL (SEQ ID NO 19) and R28TOTAAL (SEQ ID NO 20).

Figure 5 represents an alignment of the different *Candidatus Helicobacter suis* sequences. The reference sequence is RBXA001 (SEQ ID NO 2). The other sequences are 4AXA001 (SEQ ID NO 21), 6W05001 (SEQ ID NO 22), V140001 (SEQ ID NO 24).

0 EXAMPLES

Material and Methods

Samples from cattle

[0078] Seven abomasal stomachs from clinically healthy slaughtenhouse cattle originating from different Belgian and Dutch farms, were selected. The stomachs were opened longitudinally along the greater curvature and rinsed gently with tap water. Two small mucosal fragments were taken from each stomach, one near the torrus pyloricus and one in the fundic region, and were tested for urease activity (CUTest, Termire Pharma) for hat 37° C. Three mucosal biopsies from the pyloric region were taken for immunohistochemistry and in situ hybridisation and placed into 4% buttered formaline for 24 hours. For electronmic recopy, a pyloric sample was taken from the same region and fixed in eacodylate butter (0.1 M, PH 7.0) containing 6% glutariadelyde and 0.15% (Wolvo) uthenium red. From each stomach a mucosal fragment was also taken for PCPB analysis, placed into sterile PBS and frozen in liquid nitrogen. Special care was taken during sampling to avoid cross-contamination.

Samples from pigs

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[0079] Stomachs from 5 healthy slaughterhouse pigs were selected, all originating from different farms in Belgium and the Netherlands. The stomaches were opened longitudinally along the greater curvature and rinsed gently with tap water. A small mucosal fragment was taken from each stomach near the torus pyloricus and placed into an urease test tube (CUTest, Termirer Pharma) for 2 hours at 37 °C. Mucosal biopsies from the entiral part of the stomach were taken along the curvature ampror (n=2) and the curvature minor (n=2) for immunohistochemical evaluation and placed into 4 % buffered formatin. For electronmicroscopy, samples were taken from the same places and fixed in 0.1 M caccolylate buffer (pH 7.0) containing 5% glutrarisdhyde and 0.1 5% (wwton) uthlemin rect. Of ceach stomach a mucosal fragment was also taken for PCR, placed into sterile PBS and frozen in liquid nitrogen. Special care was taken during sampling to govid crose-scontamination.

Reference strains for *Candidatus Helicobacter bovis*

[0080] A total of 15 Helicobacter strains and 1 Wollinella succinogenes strain were used to test the specificity of the "Candidatus Helicobacter boxis" specific PCR (Table 1). Strains were grown on a 5 % Mueller-Hinton blood agar and incubated at 37 °C in a microaerophilic atmosphere containing approximately 5 % O₂, 3.5 % CO₂, 7.5 % H₂ and 84 % N2. Bacteriological purity was checked by plating and Gram-staining.

Reference strains for "Candidatus Helicobacter suis"

[0081] A total of 15 Helicobacter strains were used to test the specificity of the "Candidatus Helicobacter suis"-specific PCR assay (Table 1). Strains were grown on a 5% Mueller-Hinton blood agar and incubated at 37 °C in a microaerobic atmosphere containing approximately 5 % O₂, 3.5 % CO₂, 7.5 % H₂ and 84 % N₂. Bacteriological purity was checked by plating and Gram-staining.

Immunohistochemistry

[0082] Immunchistochemical staining was performed to assess the presence of Helicobactor-like organisms. Formalin-fixed samples were dehydrated and parafflin-embedded. Sections of 4 µm were made of the parafflin-embedded tissues and were placed on 3-aminopropyfitethoxysilane-ocated sides (APES, Sigma-Aldrich) and dried overnight at 60 °C. After dewaxing with xylene and rehydration in graded series with eithanol and distilled water, sections were placed in citate buffer 0.1M with 2% uneuml and were boiled (1. x3 min. 2. x5 min) in a 800 Watth incrowave over

(Whitpool M611) to alicit antigen retrieval Sides were then incubated with 12 % hydrogenperoxide in methanol (30 min) in order to block endogenous peroxidase activity. Thereafter the sides were pre-incubated with 30% normal goal serum in PBS for 30 min to reduce non-specific antibody binding. A mouse polyclonal antibody directed against H pytori (DAKO), dirtuted 1720 in PBS, was incubated ownightia 21 % for a most charmber. The sections were washed and incubated with biolinylated swine anti-rabbit immunoglobulins at 21 % for 30 min and after rinsing covered with perioxidase conjugated streptavien's boilen complex (ABC). Peroxidase activity was developed using Ho₂O₂ with diaminobenzidine (DAB) as a chromogen (Fast DAB Tablet Set, Sigma-Aktrich). Subsequently, the sections were counterstained with Mayer's hematoxylin and mounted, as a negative control, the primary artibody was replaced with fetal cell serum in Tris-HCI buffer (pH 7.6). As a positive control, a section of a mouse stomach experimentally infected with Heilobacher archivil Ma 7.599 was used

Transmission electronmicroscopy

[0083] For "Candidatus Helicobacter bovis", three different pyloric samples were selected for electrommicroscopic of evaluation based upon the high presence of Heicobacter like organisms in the corresponding immunostatiend sensions. [0084] For "Candidatus Helicobacter suis", two different antral biopsies were selected for electrommicroscopic evaluation based on the high presence of gastrospirillum-like organisms in the corresponding immunostatinad sildes. [0085] After dehydration in a graded series of actone weshes, the samples were embedded in Spurt low-viscosity resin. Ultrathin sections were poststained with uranyl acetate and lead citrate and examined with an electrommicroscope of Phillips 201 TEM) at an acceleration voltage of 60 kV.

DNA-extraction

[0086] DNA was isolated from the scrapings of the gastric biopsies and from the reference strains by lysis with quanidinium isothiocyanate and DNA was bound to silica particles according to the method of Boom et al. (1990).

Primers and PCR amplification of 16S rDNA

- [0087] Broadrange primers H33f, H61f and H1368r were selected from rRNA superfamily VI (Helicobacter, Campylobacter, Wolinella) specific regions of the 16S rRNA gene (Table 2).
- [0088] The use of broad range primer 1492RPL was suggested by Weissburg et al. (1991). A genus Helicobacterspecific primer H274f was adapted from primer 274r described by Dewhirst et al. (1994) (Table 2). Primer combinations H33F-H1368r, H274f-1492RPL and H61f-1492RPL were used to amplify a ~ 1.3-Kb, ~ 1.2-Kb and a ~ 1.4-Kb fragment of "Candidatus Helicobacter suis" respectively.
- 35 [0089] PCR reactions were performed in a volume of 50 pl containing 10mM Tris HCI (pH 8.3), 50 mM KCI, 3.5 mM MgCl₂ 200 pM of each deoxynucleoside triphosphate, 1.5 U of AmpliTaq Gold (Perkin-Etmer, Roche Molecular Systems) and 25 pmol of both forward and reverse primer (Eurogentec). Reactions were covered with mineral oil and PCR was performed in a Blomed-50 thermocycler under the following conditions: 9 min priencubation at 94 °C to activate AmpliTaq 60di, followed by 50 cycles of 30 as 49 °C, 65 as 55 °C and 45 s at 72 °C. Final extension was performed to 12 °C. DNA-extractions of Holicobacter acinonychis LMG 12684 T and Helicobacter mustelse LMG 8776 were used as positive controls.

Analysis of amplified samples

- [0090] PCR products were separated on 1 % agarose gels and stained with ethidium bromide.
- [0091] DNA-extractions of H. acinonychis LMG 12684[†] and H. musteliae LMG 8776 were used as positive controls.
 [0092] In order to determine whether PCR products were derived from Helicobacter-like organisms, the desired DNA-
- bands were cut from the gels, diluted 1/2 in distilled water and sequenced using the H33f and H1368r5-Indocarbocyanin (Cy5) for 'Candidatus Helicobacter bovis' and respectively H61f and 1492HPL Indocarbocyanin (Cy5) labeled for 50 "Candidatus Helicobacter suis" Partial sequences users exceeded for homologous sequences using the R016 EN-
- *Candidatus Helicobacter suis*. Partial sequences were screened for homologous sequences using the NCBI GEN-INFO ® BLAST Network service (http://www.ncbi.nlm.nih.gov/BLAST/) (Allshul et al., 1997).

DNA cloning and sequence analysis for "Candidatus Helicobacter bovis"

55 [0093] PCR amplimers comprising the 16S rDNA-sequences derived from four different stomach samples (R2, R3, R5, R6) were each cloned into plasmid vector pGEA-T (Promage Biotech) according to the manufacturer's instructions and transformed into Escherichia coli MM09 using standard procedures. Plasmids were purified using the Easy Prep. Plasmid Proparation Kit (Pfarmacia Biotech). Sequences were determined by the T7-sequencing system (Pharmacia).

Biotech). Two primers flanking the multiple cloning sites (T7, SP6) as well as internal primers H390f and H1053r were used (Table 2). The sequence derived from the clone of the F2 sample (F2XA) was used as reference sequence. This sequence was has been asigned Genbank Accession No. AF127028. Sequence analysis was performed with the PCGene software (Infelligenetics)

5 [0094] PCR amplicons of three other gastric samples (R13, R27, R28) were sequenced without prior cloning (referred to below as direct sequence analysis).

DNA cloning and sequencing for "Candidatus Helicobacter suis"

(9065] PCR amplimers comprising the 16S rONA-sequences from 2 different stornache (V2B, V4A) were cloned into plasmid vector pGEM-T (Promega Biotech) according to the manufacturer's instructions and transformed into Escherichia coii JM109 using standard procedures. Plasmids were purified using the Easy Prep Plasmid Prep Kit (Pharmacia Biotech), Sequences were determined by the 17-sequencing system (Pharmacia Biotech). Two primers flanking the multiple cloning sites (T2 and SP6) as well as internal primers #380/rand H052 were used (Table 2), Sequence analysis was performed with the PCGene software (intelligenetics). A reference sequence was determined based on its high length and was compared to the new sequenceve and the other derived sequences, to check its integrity (see Figures 4 and 5). The reference sequence V2EXA was assigned Genbank Accession No. AF127028.

[0096] PCR amplicons of three other gastric samples (V5, V14, V19) were sequenced without prior cloning (referred to below as direct sequence analysis).

Phylogenetic analysis for "Candidatus Helicobacter bovis"

an

[0097] Phylogenetic analysis was performed using the GeneCompar 2.0 software package (Applied Maths). Sequences of strains belonging to the spelion subdivision (Table 3) were retirieved from the BIBL data library and were aligned with reference sequence R2XA. A similarity matrix was constructed from the aligned sequences and was corrected for multiple base changes by the method of Jukes & Cantor (1969). Unknown bases and gaps were not considered in the numerical analysis. Aphylogenetic tree was constructed using the neighbour-joining method of Saltou & Nei (1987).

Phylogenetic analysis for "Candidatus Helicobacter suis"

[0098] Phylogenetic analysis was performed using the GeneCompar 2.0 soltware package (Applied Maths). All five "Candidatus Helicobacter suis" sequences and the sequences of strains belonging to the same phylogenetic lineage (Table 3) were aligned. Using the neighbour-joining method, a phylogenetic tree and corresponding similarity matrix was constructed. Unknown bases and gaps were not considered in the numerical analysis

"Candidatus Helicobacter bovis" specific PCR-assay

[0099] "Candidatus Helicobacter bovis" specific oligonucleotides R574f and R832f (Table 2), were selected from variable rDNA regions of the sequences determined by direct and indirect sequence analysis. These primers comprised a 259 bp 165 rDNA-fragment and were used to develop a specific PCR and an in situ hybridisation procedure. Within this fragment an internal "Candidatus Helicobacter bovis" specific probe R628f (Table 2) was selected for southern both hybridisation purposes.

[0100] PCR reactions were performed in a volume of 50 µl containing 10 mM Tris HCl (pH 8.3), 50 mM KCl, 25 mM MgCl₂, 200 µM of each deoxynucleoside triphosphate, 1.5 U of AmpliTaq Gold, and 25 pmol of both forward and reverse primer. PCR amplification was performed under the following conditions: 9 min preincubation at 94 °C to activate AmpliTaq Gold, followed by 40 cycles of 30 s at 94 °C, 45 s at 60 °C and 90 s at 72 °C. Final extension was performed for 5 min at 72 °C. All gastric DNA-extracts were tested with this PCR. For positive controls, plasmid DNA was used from the cloned 165 fONA fragments (R2XA), As a negative control a DNA-extract was used from an abomasum of lacking of Heiocoacter/like organisms.

[0101] Specificity of the *Candidatus Helicobacter bovis* specific oligonucleotides R574f and R832r was tested by PCR using DNA-extracts of 15 different Helicobacter strains and a Wolinella succinogenes strain (Table 1).

[0102] PCR products were separated on 2% agarose gels, stained with ethicium bromide and transferred to Hybord
N+ (Amershamly be lector-elution. Southern bits thylindisation was performed with the [h²⁹²] ATE labelled probe R628f (Table 2) according to standard procedures (Amersham Pharmacia Bistech). In order to ensure the specificity of the probe hybridisation, bitsia were washed twice with 0.1 x SSC + 0.1 % SDC at SSC.

"Candidatus Helicobacter suls" specific diagnostic PCR-assay and Southern blot hybridisation

[0103] **Candidatus* Helicobacter suis** specific primers (M82f and V128f) were selected from variable rDNA regions of the sequences determined by direct and indirect sequence analysis, comprising a –0.4 kb 16sr DNA-fragment. Within this fragment a **Candidatus* Helicobacter suis** specific probe V1000f (Table 2) was selected for hybridisation purposes. PCR reactions were performed in a volume of 50 pl containing 10 mM fris HCl (pH 8.3), 50 mM KCl, 2.5 mM MgCl₂, 200 µM of each deconvuoleoside trybosphate, 1.5 U of AmpliTiag Gold (Perkin-Elmon, and 25 pmol of both forward and reverse primer (Eurogentec). PCR amplification was performed under the following conditions: 9 min preincubation at 94 °C to activate AmpliTiag Gold, followed by 40 cycles of 30 at 94 °C, 45 at 60 °C and 90 s at 72 °C. Final axtension was performed to 5 min at 72 °C. As a positive control, plasmid DNA was used from the cloned 15sr 10NA fragments (V2B, V4A). As a negative control DNA extracted from the stomach of a gnotobiotic piglet was used.

[0104] To test the specificity of the primers, PCR was also performed on DNA-extracts of 15 different Helicobacter species. (Table 1).

[0105] PCR products were separated on 2% agarose gels, stained with ethicilium bromide and transferred to Hybond N+ (Amersham) by electro-blotting. Southern blot hybridisation was performed with the [x²²⁷] ATP-labelled probe V1000f according to standard procedures (Amersham Pharmacia Biotech). In order to ensure the specificity of the probe hybridisation, blots were washed twice with 0.1 x SSC + 0.1 % SDS at 55°C.

20 In situ hybridisation for "Candidatus Helicobacter bovis"

[0168] In order to make the link between the "Candidatus Helicobacter bowis" specific probe and the bacterial spiral cells observed in the tissue sections, an in situ hybridisation procedure was performed on the formalin fixed and paraffin embedded pyloric samples of each animal. A 259-base digoxigenin-labeled probe was synthezized using the "PCA Dig Probe Synthesis Kit" (Boehringer Mannheim) in combination with the "Candidatus Helicobacter bowis" specific primers R574 and R5827 (Table 2). PCR conditions were identical to those described in the diagnostic PCR assay. The resulting PCR product was purified using the "High Pure PCR Product Purification Kit" (Boehringer Mannheim) following manufacturers' instructions.

[0107] To avoid RNA'se activity, all glassware was heated at 160°C for 3 hours. Further procautions included the use of RNA'se-free water, and the use of tentil disposable materials whenever possible. Socions of the paraffilm-embodded tissues (4 µm thick) were mounted on RNA'se-free, APES-coated sides (Sigma-Aldrich) and fixed by heating for 1 hour at 60°C. The sections were deparaffinized in xylene (2x5 min), rehydrated through graded ethanol, and washed livice in PBS for 5 min each. Sections were then treated with proteinase K (DAKO) for 15 min each at 3°°C in a huntifilited chamber. The enzyme was inactivated by treatment with 0.2 % glycine in PBS for 5 min each, dehydrated in graded ethanol and air dired. Tissues were circumlined with a DAKO Pen (DAKO) to avoid liquid spillage during further processing and to ensure an efficient sealing of the coversity. For the hybridisation step, sections were covered with 5 to 15 pt solution, containing 5 nglyl labeled probe in 50° delorized formamide, 2x 5°CC, 10 % destran sultate, 0.25 µg/Ju yeast t-RNA, 0.5 µg/Ju heat denatured salmon sperm DNA, and to Danhart's solution. Sections were overed with a pice of coversity to avoid evaporation. To denature the probe, sections were heated for 10 min at 55°C and chilled on ice for 10 min. Slides were then hybridised overnight at 3°C in a hundflided chamber. To remove the unbound probe, he coversity were removed and the sections were washed in 2x SCC and ta SCC at com temperature for 10 min each followed by two washes of 0.3x SCC at 40°C for 10 min and at com temperature for 10 min expectively.

[0108] All steps involving the immunological detection of the hybridised probe were performed at room temperature. The sections were treated list for 30 minutes in Buller 1 (100mM Tris HCI, 150 mM NaCl, pH 7.5) containing 2.9 normal goat serum and 0.3 % Triton X-100. An incubation step followed for 3 hours with diluted (1:30 in the same solution) anti-digoxigenin antibodies conjugated honese-radiath peroxidase (DAKC). Unbound artibodies were washed gently on a sharker with Buller 1 followed by Buller 2 (100 mM Tris HCI, 100 mM MpCI, 50 mM MpCI, pH 5.5) for 15 min each. To optimize the detection level, the "Tyramid Signal Amplification System" (NEN Life Science Products) was applied on each section, Ioliving manufacturers instructions. The hybridised probe was then visualized, using It-Q2 with diaminobenzidine as a chromogen (Fast DAB Tablet Set, Sigma-Aldrich). Thereafter the sections were counterstained with Maver's hematoxylin and mounted.

In situ hybridisation for "Candidatus Helicobacter suis"

[0108] To link the derived sequence to the corresponding organism, an in situ/hybridisation procedure was performed on the formalin fixed and paraffin embedded pyloric samples of each animal. A -0.4 Kb digoxigenin-labeled probe was synthezised using the "PCP Dig Probe Synthesis Kit" (Boehringer Mannheim) in combination with the "Candidatus

Helicobacter suis*-specific primers V832I and V1261r (Table 2). The rest of the method was performed as mentioned above for *Candidatus Helicobacter bovis*.

Nucleotide sequence accession numbers

[0110] Accession numbers of the 16S rDNA gene sequences used for the phylogenetic analysis are listed in table 3. [0111] The 16S rDNA nucleotide sequence of "Candidatus Helicobacter bovis" has been deposited in the Genbank database, under accession number AF12702.

[0112] The 16S rDNA nucleotide sequence of "Candidatus Helicobacter suis" has been deposited in the Genbank database under accession number AF127028.

Results

Urease activity and immunohistochemical evaluation for the cattle samples

[0113] Urease activity was observed in all pyloric samples (7/7). In the fundic samples, urease activity was absent (0/7) Spiral immunostained organisms were observed in the pyloric samples. The highest concentration was seen in the most distal pyloric samples. They were mostly situated in the mucus layer and in the fluend of the proximal part of the gastric crypts where they formed small clusters. In some samples, coccoid organisms, were observed between the spiral bacteria, which also crossreacted with the H. Pylori polyclonal antibodies. In the positive control only Heldozader pylori - file bacterial were stained while in the negative controls on staining was observed.

Urease activity and immunohistochemical evaluation for the pig samples

[0114] Tightly colled immunostained spiral organisms, morphologically similar to 'Gastrospirillums usir' (Culeric et al., 1990) were observed in all stomache (SFS), which was consistent with the presence of urease activity (5FS). The gastrospirillum-like organisms were seen laying separately or in small clusters with a patchy distribution over the sample, and were found mostly in the superficial part of the gastric crypts. Some bacteria reveated blogal mimunostained lagellae. Immunostained coccold-like organisms were also observed in the pyloric crypts. In the positive control, only Helicobacter, only high scale risk were standed while in the negative control to labeling was observed.

Transmission electronmicroscopy for "Candidatus Helicobacter bovis"

[0115] Large groups of multiple spiral bacteria were seen within the crypts of the gastric mucosa. There was no obvious cell association between the bacteria and the gastric cells, neither were there any intracellular bacterial inclusions. The bacterial were helical-shaped and had 1-3 complete spiral turns per cell with a wavelength of approximately 750 nm. Cells were 1 - 2.5 µm long and 0.3 µm wide. At least four lagelles were seen at one end. It was unclear whether these flagellae were unit or bipolar, neither could the presence or absence of a flagellae what he be noted.

Transmission electronmicroscopy for "Candidatus Helicobacter suis"

[0116] Within the gastric crypts of the antral region, knogludinal and transversal sections of spiral organisms could be seen. All bactoria had the same characteristic lightly colled appearance, typical of Indicated rewith the gastrospirillum morphology. The length of cells varied from 2.5 to 3.5 pm and they were approximately 0.6 pm wide. Multiple complete spiral turns with a wavelength of 1.6 00 nm were seen in all longitudinal sections. As only fee studied although partial fragments were observed. The bacteria were observed. The bacteria were not seen intracellularly nor was there any obvious cell association with the surrounding epithelial cells. The presence or absence of a flagella shadeh to could not be noted.

50 Amplification, cloning and sequencing of Helicobacter-like 16S rDNA fragments from cattle samples

[0117] PCR amplification of the 165 rRNA gene using the H33f and H1368r primers, produced a fragment of the expected size range (± 1.3 kb) in all seven samples examined. Partial direct sequence analysis of low of these bands (P2, R3, R5, R6) and subsequent database comparison (BLAST) confirmed the PCR products to be Helicobacter-like 165 r(DNA fragments. Four PCR products (R2, R3, R5, R6) were cloned followed by partial screening. In one clone a Costridium-like 165 r(DNA regenent was found. In all other clones Helicobacter-like fragments were inserted. The 165 r(DNA asquances of four clones derived from different animals (R2XA, R3XA, R5XE, R6XA), were determined. Additional sequences of three other samples (R13, R2, R28) were characterized by direct sequence analysis using the

primers H33f, H1368r, H390f and H1053r.

Amplification, cloning and sequencing of Helicobacter-like 16S rDNA fragments from pig samples

10 Sequences and phylogenetic analysis for cattle samples

[0119] Sequence length varied from 1287 to 1335 basepairs. Pairwise comparisons between these 7 sequences revealed a sequence hormology of more han 99 %. One relatence sequence (R2XA) of 1335 bp (see Figure 1: SEQ IDN O1) was selected for phylogenetic evaluation. A similarity matrix based on comparisons of 165 rRNA sequences of 23 strains representing all validly named Helicobactor species, *Helicobactor helimanni* (type1, type2), Campylobactor joint, *Carobactor representing all validly named Helicobactor see sea calculated, by this analysis it was shown that the sequences of the bovine Helicobactor-like organisms form a distinct group within the genus Helicobactor with Helicobactor bills as closest taxonomic relative (level of similarity 92.8%). The reference sequence was clearly distinct from sequences belonging to other superlamily VI genera, as shown by a 85.6, 85.1 % and 93.7 % homology with Campylobactor joinn, *Acobactor buttleri and Wolfinella succinogenes respectively. A phylogenetic tree based on this analysis is shown in Fig. 3A.

Sequences and phylogenetic analysis for pig samples

25 [0120] The 5 sequences that were determined had lengths varying from 1345 to 1421 basepairs. Pairwise comparisons between 1345 bp consensus fragments of these sequences, revealed an ininium homology of 97.7 % one reference sequence of 1421 bp, obtained from PCR product 28KA (see Figure 2. SEO ID NO 2), was used for phylogenetic analysis. A similarity matrix was calculated based on comparisons of 165 rDNA sequences of all Heliochers species. *Heliocheater Inequality 1992 and type 2, Campylobacter jojuni, Arcobacter butzien and Wolfmellas succincymers (Table 3). In this analysis, the sequence of the porcine gastrospirillum-like organism formed a district subgroup within the Heliocheater Inequality 1992 to the regastrospirillum-like pacterial. *Heliocheater Inequality 1992 to 164 for gastrospirillum-like bacteria, *H. Idis., *H. bizzozoronii, H. salchmonis, *H. heliniannii* type 1 (devel of similanty) 99.5 %. The similarity level of other gastrospirillum-like bacteria, *H. Idis., *H. bizzozoronii, H. salchmonis and H. heliniannii* type 2 was 96.4 %, 96.5 %, and 96.8 % respectively. The reference sequence was clearly distinct from sequences belonging to other superfamily Vi-penara, as shown by a 86.2 %, 84.7 %, and 99.6 % homology with *Campylobacter jejuni, *Arcobacter butzleri and Wolfinellas succincipenes respectively.

Diagnostic PCR-assay for "Candidatus Helicobacter bovis"

[0122] A 259 base fragment was produced for all seven stomach samples with primer pair R574/R822/. All PCR products crosshybridized with the R628/probe after southern blot hybridisation. No amplification product was obtained using DNA preparations from any of the Helicobacter strains, nor from the bovine Wolfinella succinogenes strain (Table 1). The positive control yielded a ~0.3 Kb product as expected. There was no DNA-amplification using the negative control material.

"Candidatus Helicobacter suis"-specific PCR and Southern blot hybridisation

[0123] Amplification of Helicobacter DNA using the primers V822f and V126fr produced a 433-base fragment from all five stomach samples. All PCR products hybridised with the V1000f probe after Southern blot hybridisation. No amplification product was obtained using DNA preparations from any of the Helicobacter strains including H. Palis, H. bizzozoronii and H. salomonis (Table 1), nor from the negative control. PCR with the cloned reference material (2BXA) yielded a – 0.4 Kb product as expected.

In situ hybridisation for "Candidatus Helicobacter bovis"

[0124] In situ hybridisation of the bovine Helicobacter-like bacteria with the "Candidatus Helicobacter bovis" - specific probe was seen in sections from all (7/7) stomachs. These bacteria were observed as darkbrown spiral organisms,

organised in small clusters, situated in the gastric crypts of the pyloric part of the abomasal stomach. Not all spiral bacteria were stained Sometimes a faint background, seen as fine stained strings, was observed in the surrounding cells. This background staining was also observed in the H. pylori-infected mouse stomach which was used as a negative control. The H. pylori cells in this control though did not hybridise with the "Candidatus Helicobacter bovist-specific probe."

In situ hybridisation for "Candidatus Helicobacter suis"

[0132] In situ hybridisation of "Gastrospirillum suis"-like bacteria with the "Candidatus Helicobacter suis": specific probe was seen in sections from all (5/5) stomachs. Bacteria were observed as darthrown spiral organisms in the superficial mucus layer and the gastric crypts. In some cases, helical organisms located deeply in the crypte, were weakly labeled or were negative. Sometimes a faint background, seen as fine stained strings, was observed in the surrounding cells. This background takining was also observed in the H. pyl-infected mouse stomach which was used as a negative control. The H. pyl-ori cells in this control though did not hybridise with the "Candidatus Helicobacter suis" specific probe.

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Table 1:

	Table 1.				
Bacterial strains used for the evaluation of the *Candidatus Helicobacter bovis* specific PCR					
Taxon	Source	Collection N° or Strain			
Helicobacter acinonychis	Cheetah gastric mucosa	LMG 12684 ^T			
Helicobacter cinaedi	Human feces	LMG 7543 T			
Helicobacter sp. strain CLO-3	Human rectal swab	LMG 7792			
Helicobacter fennelliae	Human feces	LMG 11759			
Helicobacter pametensis	Tern feces	LMG 12678 T			
Helicobacter sp. strain Bird B	Bird feces	LMG 12679			
Helicobacter sp. strain Bird C	Bird feces	LMG 13642			
Helicobacter hepaticus	Murine liver	LMG 16316 ^T			
Helicobacter pullorum	Chicken lower bowel	LMG 16318			
Helicobacter mustelae	Ferret gastric mucosa	LMG 18044 T			
Helicobacter canis	Canine feces	LMG 18086 T			
Helicobacter muridarum	Murine intestinal mucosa	LMG 14378 T			
Helicobacter bizzozeronii	Canine gastric mucosa	Strain 12A			
Helicobacter salonionis	Canine gastric mucosa	CCUG 37845 T			
Helicobacter felis	Feline gastric mucosa	CCUG 28539 T			

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Table 2: Oligonucleutide primers and probe used for PCR amplification, sequencing of genes coding for 16S rRNA and Southern blot hybridisation

10	Primers	Sequences (5'-3')		Escherichia coli 16S rRNA position		
	нззг	ACG CTG GCG GCG TGC CTA ATA CAT GCA AGT CG		(SEQ ID		
15	H1368r	GGT GAG TAC AAG ACC CGG GAA CGT ATT CAC CG	1368-1388 (SEQ NO 4)			
20	H390f	GCA GCA ACG CCG CGT GGA GGA TGA		(SEQ ID		
25	H1053r	ACG AGC TGA CGA CAG CCG TG	1053-1072 (SEQ I			
30	R574f	AGA GCG TGT AGG CGG AAT GAT		(SEQ ID		
	R628f	AAC TGC GTT TGA AAC TAT CAT T		(SEQ ID		
35	H61f	TGC AAG TCG AAC GAT GAA GC		(SEQ ID		
40	H274f	AGG CTA TGA CGG GTA TCC GGC CTG AGA		(SEQ ID		
45	1492RPL	GCC GCC CGG GTT ACC TTG TTA CGA CTT		(SEQ ID		
50	V832f	TTG GGA GGC TTT GTC TTT CCA		0 (SEQ ID 12)		
	V1261r	GAT TAG CTC TGC CTC GCG GCT		1 (SEQ ID 13)		

V1000f		AGG AAT TCC CTA GAA ATA GGG	1000-1020 (SEQ ID NO 26)		
,	R832r	CGA GGA GAC AAG CCC CCC GA	832-851 (SEQ ID NO 14)		

Table 3:

Taxon	Source	Genbank Accession No		
"Gastrospinillum hominis" type 1	Human gastric mucosa	L10079		
"Gastrospirillum hominis" type 2	Human gastric mucosa	L10080		
Helicobacter acinonychis	Cheetahgastric mucosa	M88148		
Helicobacter bilis	Murine liver	U18766		
Helicobacter bizzozeronii	Canine gastric mucosa	Y09404		
Helicobacter canis	Canine feces	L13464		
Helicobacter cholecystus	Murine liver	U46129		
Helicobacter cinaedi	Human feces	, M88150		
Helicobacter felis	Feline gastric mucosa	M57398		
Helicobacter fennelliae	Human feces	MBB154		
Helicobacter hepaticus	Murine liver	U07574		
Helicobacter muridarum	Murine intestinal mucosa	M80205		
Helicobacter mustelae	Ferret gastric mucosa	M35048		
Helicobacter nemestrinae	Macaque gastric mucosa	X67854		
Helicobacter pametensis	Swine feces	MBB 155		
Helicobacter pullorum	Broiler chicken cecum	L36141		
Helicobacter pylori	Human gastric mucosa	M88157		
Helicobacter salomonis	Canine gastric mucosa	Y09405		
Helicobacter trogontum	Rat colon mucosa	U65103		
Helicobacter rodentium	Murine intestinal mucosa	U96297		
Arcobacter butzleri	Human	L14626		
Campylobacter jejuni	Human feces	L14630		
Wolinella succinogenes	Cattle abomasal mucosa	M88159		

Annex to the application documents - subsquently filed sequences listing

[0185]

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Claims

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- 1. An isolated 16S rDNA Helicobacter polynucleic acid sequence selected from any of the following
- 30 (a) a sequence represented in any of SEQ ID NO 1 to 2, or, the 16S rRNA sequence encoded thereby,
 - (b) a sequence which hybridizes under stringent conditions to any of the sequences defined in (a).
 - 2. An isolated polynucleid acid sequence according to claim 1 represented by any of SEQ ID NO 1 to 2 or 15 to 24.
 - An isolated polynucleic acid sequence according to claim 1 which is more than 92.8%, preferably more than 93.5%, more preferably more than 95% and most preferably more than 97.5% homologous to SEQ ID NO 1.
 - A part of an isolated polynucleic acid according to any of claims 1 to 3, wherein said part is unique to the polynucleic acid sequence it is derived from.
 - 5. A probe which specifically hybridizes to a polynucleic acid sequence according to any of claims 1 to 4.
- 6. A primer which specifically amplifies a polynucleic acid sequence according to any of claims 1 to 4.
 - A method for detection and/or typing of Helicobacter strains present in a biological sample comprising hybridizing
 the 16S rRNA gene target region polymuclootides of said Helicobacter strains present in said biological sample
 with at least one probe according to claim 5.
- 59 8. A method for detection and/or typing of Helicobacter strains present in a biological sample comprising specifically amplifying the 15S rRNA gene target region polynucleotides of said Helicobacter strains present in said biological sample with at least one primer according to claim 6.
 - A method for detaction and/or typing of Helicobacter strains present in a biological sample comprising specifically hybridizing or specifically amplifying the 15S rRNA gene target region polynucleotidas of said Helicobacter strains present in said biological sample with at least one sequence which is more than 96.6% homologous to SEQ ID NO 2, or a sequence specific primer or a sequence specific probe derived thereof.

- 10. A diagnostic kit for detection and/or typing of Helicobacter strains comprising:
 - at least one probe according to claim 5 or 9, and/or,
- at least one primer according to claim 6 or 9.

15

30

- 11. A medicament comprising a polynucleic acid sequence according to any of claims 1 to 6.
- 12. A polynucleic acid sequence according to any of claims 1 to 6 for use as a medicament.

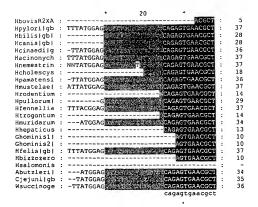


Figure 1 - 1

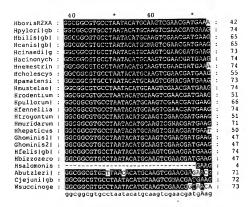


Figure 1 - 2



Figure 1 3

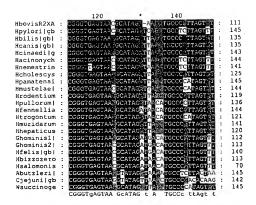


Figure 1 - 4

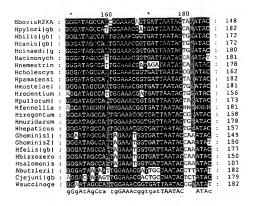


Figure 1 →

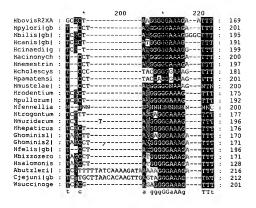


Figure 1 - 6

		•	240	*	26		
HbovisR2XA	:					:	-
Hpylorilgb	:					:	-
Hbilis gb	:	CAATAAAGAA	TTTCTCTTTTTA	GTGCTTTGTG	TTGTT	:	232
Hcanis gb	:					:	-
Hcinaedilg	:					:	-
Hacinonych	:					:	-
Hnemestrin	:					:	-
Hcholescys	:					:	-
Hpamatensi	:					:	-
Hmustelae	:					:	-
Hrodentium	:					:	-
Hpullorum	:					:	-
Hfennellia	:					:	-
Htrogontum	:					:	-
Hmuridarum	:					:	-
Hhepaticus	:					:	-
Ghominis1	:					:	-
Ghominis2	:					:	-
Hfelisigbl	:					:	-
Hbizzozero	:					:	-
Hsalomonis	:					:	-
Abutzleri	:					:	-
Cjejunilgb	:					:	-
Wsuccinoge	:						_

Figure 1 - 7

		0	*	280	*		
HbovisR2XA	:					:	-
Hpylori qb	:					:	-
Hbilis qb	:	GGCACAAAA	TCTAGTA	TTTGGAATGAGA	AATTGATG	:	269
Hcanislabl	:					:	-
Hcinaedilg	:					:	-
Hacinonych	:					:	-
Hnemestrin	:					:	_
Hcholescys	:					:	-
Hpamatensi	:					:	-
Hmustelael	:					:	-
Hrodentium	:					:	-
Hpullorum	:					:	-
Hfennellia	:					:	-
Htrogontum	:					:	-
Hmuridarum	:					:	
Hhepaticus	:					:	-
Ghominisl	:					:	-
Ghominis21	:					:	-
Hfelis gb	:					:	-
Hbizzozero	:					:	-
Hsalomonis	:					:	-
Abutzleri	:					:	-
Cjejunilgb	:					:	-
Wsuccinoge	:					:	-

Figure 1 - 8

		300	*	320	*		
HbovisR2XA	:					:	-
Hpylori gb	:					:	-
Hbilis qb	:	TTGTGAAG	CAATTTGTG	CGGAGACTAGA	CTTAGTGTC	:	306
Hcanis qb	:					:	-
Hcinaedi q	:					:	-
Hacinonych	:					:	_
Hnemestrin	:					:	-
Hcholescys	:						-
Hpamatensi	:					:	_
Hmustelael	:						_
Arodentium	:					:	_
Hpullorum	:					:	-
Hfennellia	:					:	_
Htrogontum	:					:	-
Hmuridarum	:					:	-
Hhepaticus	:		·			:	-
Ghominis1	:					:	-
Ghominis2	:					:	-
Hfelisigbi	:					:	-
Hbizzozero	:					:	-
Hsalomonis	:					:	-
Abutzleri	:					:	-
Cjejunilgb	:				·	:	-
Wsuccinoge							_

Figure 1 - 9

		340	*	360			
HbovisR2XA	:					:	-
Hpylori gb	:					:	-
Hbilis gb	:	TGTCGCACAAG	CAAATTGCG	AACTCATCGATT	TATCG	:	343
Hcanis gb	:					:	-
Hcinaedilg	:					:	-
Hacinonych	:					:	-
Hnemestrin	:					:	-
Hcholescys	:					:	-
Hpamatensi	:					:	_
Hmustelael	:					:	-
Hrodentium	:		-			:	-
Hpullorum	:					:	-
Hfennellia	:					:	-
Htrogontum	;					:	-
Hmuridarum	:					:	-
Hhepaticus	:					:	-
Ghominisl	:					:	-
Ghominis2	:					:	-
Hfelis gb	:		·	- -		:	-
Hbizzozero	:					:	-
Hsalomonis	:					:	-
Abutzleril	:					:	-
Cjejunilgb	:					:	-
Wsuccinoge	:					:	-

Figure 1 - 10

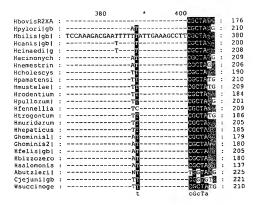


Figure 1 - 11

		*	420	*	440		
HbovisR2XA	:	GGAT G	CTATGTCCT	ATCAGCTAG	TTGGTGAGGTA	:	213
Hpylori qb	:	AGAT AG	CTATGTCC:	ATCAGCTTG	TTGGTAAGGTA	:	247
Hbilis qb	:	GGAT	CTAIGTOOT	ATCAGCTTG	TIGGTGAGGTA	:	417
Hcanis qb	:	GGATT::\}G	CTATGTCC:	ATCAUCTEG	TTGGTGAGGTA	:	237
Hcinaedilg	:				TTGGTGAGGTA	:	245
Hacinonych	:	ACAT: C	CTATECCT	ATCAGCTTG	TTEGTAAGGTA	:	246
Hnemestrin	:	GGAT AG	TOTATGTOO!	ATCAGOTTG	TTEGTAAGGTA	:	243
Hcholescys	:	GGATI 40	CTATGTCCT	ATCAGCTTS	TTGGTGAGGTA	:	227
Hpamatensi	:				TTOGTGAGGTA	:	247
Hmustelae	:	GGATA	#CTATGTCCT	ATCAGCTTO	TTGGTGAGGTA	:	246
Hrodentium	:				TTGGTGAGGTA	:	221
Hpullorum	:				TTGGTGAGGTA	:	238
Hfennellia	:				TTGGTGAGGTA		246
Htrogontum	:				TTGGTGAGGTA		223
Hmuridarum	:				TTGGTGAGGTA		242
Hhepaticus	:				STTGGTGAGGTA		222
Ghominis1	:				TTGGTGAGGTA		216
Ghominis2	:				TTGUTGAGGTA		217
Hfelis gb	:				TTGGTGAGGTA		242
Hbizzozero	:				TTGGTGAGGT/		217
Hsalomonis	:				TTGGCGGGGTA		174
Abutzleri	:				TTGGTGGGGTA		262 258
Cjejunilgb	:				TTGGTAAGGTA		258
Wsuccinoge	:	gGAT C			TTCGTGACGTA		241
		gom'r C	, crargteer	MICHGETE	or reorgade TA		

Figure 1 - 12

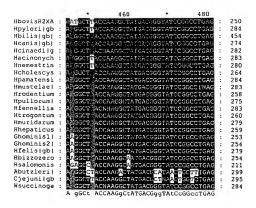


Figure 1 - 13

		*	500		5		
HbovisR2XA	:	AGGGTGARCG	GACACAC CGGAAC'	GAGAGACG	WCG G	:	287
Hpylori gb	:		GACACACTGGAACT			:	321
Hbilis qb	:	AGGGTGATCG	GACACACTGGAACI	rgagacacg(IT CCA	:	491
Heanistabl	:		SACACACTGGAACT			:	311
Heinaedilg	:		GACACACTGGAACT			:	319
Hacinonych	:		GACACACTISCARO			:	320
Hnemestrin	:	AGGGTGAYCG	GACACACTGGAACT	egycycyda.	STOCA	:	317
Hcholescys	:	AGGGTGAMCG	CACACACTGGAAC'	rgagacacgi	STCCA	:	301
Hpamatensi	:		GACACACTGGAACT			:	321
Hmustelaei	:		GACACACTGGAAC'			:	320
Hrodentium	:		GACACACTGGAAC			:	295
Hpullorum!	:		GACACACTUGAAC			:	312
Hfennellia	:		GACACACTGGAAC			:	320
Htrogontum	:		GACACACTGGAAC			:	297
Hmuridarum	:		GACACACTGGAAC			:	316
Hhepaticus	:		GACACACTGGAAC			:	296
Ghominisl	:		GACACACTGGAAC			:	290
Ghominis2	:		GACACACTGGAAC				291
Hfelis gb	:		GACACACTGGAAC			:	316
Hbizzozero	:		GACACACTGGAAC			:	291
Hsalomonis	:		GACACACTGGAAC			:	248
Abutzleri	:		GTCACACTGGAAC			:	336
Cjejunilgb	:		GTCACACTGGAAC			:	332
Wsuccinoge	:		GACACACTGGAAC			:	321
		AGGGTGA C	GaCACACtGGAAC	TGAGACACG	GTCCa		

Figure 1 - 14

		20	*	540	*		
HbovisR2XA	:	GACTOCT	ACGGGAGGC	AGCAGTAGGC	SAATATTGCTCA		324
Hpylorilab	:	GACTCCT	ADUGGRAGGO	AGCAGTAGGC	BARTATTGCTCA	:	358
Hbilis gb	:	GACTOCT	ACGUGAGGO	ACCAGINGGO	MATATTECTO	:	528
Hcanis qb	:	GACTOCT	ACGGGAAGG	AGCAGTAGGC	MARTATTOCTCA	:	348
Hcinaedilq	:	GACTOCT	ACGUGAGGO	AGCASTAGGC	SANTATIGCTOR	:	356
Hacinonych	:	GACTOCT	ROGGGAGGG	AGCAGTAGGG	AATATTGUTCA	:	357
Hnemestrin	:	GACTOUT	ACGGGAGGG	AGCASTAGGS	BAATATTGCTCA	:	354
Hcholescys	:	GACTCCT	ACGGGAGGC	AGCAGTAGG	BAATATTGCTCA	:	338
Hpamatensi	:	GACTCCT	ACGGGAGGG	AGCAGTAGG	GAATATTGCTCA		358
Hmustelae;	:	GACTCCT	ACGGGAGGC	AGCAGTAGG	BAATATTECTCA	:	357
Hrodentium	:	GACTCCT	ACGGGAGGC	AGCAGTAGG	SAATATTGCTCA	:	332
Hpullorum;	:	GACTCCT	ACGGGAGGC	AGCAGTAGG	BAATATTGCTC	:	349
Hfennellia	:	GNCTCCT	ACGGGAGGC	AGCASTAGG	GAATATTSCTC	:	357
Htrogontum	:	GACTCCT	'ACGGGAGGC	AGCAGTAGG	BAATATTGCTCA	:	334
Hmuridarum	:	GACTCCT	ACGGGAGGG	AGCAGTAGG	GAATATTGCTC/	:	353
Hhepaticus	:	GACTCCI	'ACGGGAGG	AGCAGTAGG	GAATATTGCTCA	:	333
Ghominis1	:	GACTCCT	ACGGGAGG	AGCAGTAGG	JAATATTGCTCA	:	327
Ghominis2	:				GAATATTECTC		328
Hfelis gb	:				GAATATTGCTC		353
Hbizzozero	:				GAATATTGCTC		328
Hsalomonis	:				gaatattgc <u>t</u> c,		285
Abutzleril	:				gaatattec <mark>a</mark> c		373
Cjejunilgb	:				GAATATTGC GC		369
Wsuccinoge	:				GAATATTGCTC.		358
		GACTCCT	ACGGGAGG	CAGCAGTaGG	GAATATTGCtC.	A.	

Figure 1 - 15

		560	*	580			
HbovisR2XA	: [ATGGGGGAAA				:	361
Hpylori gb	:	ATGGGGGAAA				:	395
Hbilis gb	:	ATGOGGGAAA	CCTGAAGG	AGCAACGCCG	CGTGGAGG	:	565
Hcanis gb	:	A FGGGGGAAA	CCTGAAGO	AGCA40GCCG	COTOGAGO	:	385
Hcinaedilg	:	ATGOGGCAAA	CCTGAAGC	AGCARCGCCG	COTGCAGG	:	393
Hacinonych	:	ATGGGS GAR	CCTGAAGO	AGCAACGCCG	CGTGGAGG	:	394
Hnemestrin	:	ATGGGGAAA	COTSHAGO	AGCAACGCCG	CGTGGAGG	:	391
Hcholescys	:	ATGGGCGAAA	GCTG-AGC	AGCAMONGOG	COTUGAGO	:	375
Hpamatensi	:	ATGGGCGAAA	GCCTGAAGC	RGCAACGCCG	CGTGGAGG	:	395
Hmustelael	:	ATGGG GAAA	SCCTGAAGC	AGCAACGCCG	CGTGGAGG	:	394
Hrodentium	:	ATGGG GAAA	CCTGAAGC	AGCAACGCCG	CGTGGAGG	:	369
Hpullorum	:	ATGGGGGAAA	COTGRAGO	AGCAACGCCG	CGTGGAGG	:	386
Hfennellia	:	ATGGGGAAA				:	394
Htrogontum	:	ATGGGGGAAA	GCCT GAAGO	ASCAACGCCG	CGTGGAGG	:	371
Hmuridarum	:	ATGGGGGAAA	CCTGAAGO	CAGCAACGCCC	CGTGGAGG	:	390
Hhepaticus	:	ATGGGGGAAA				:	370
Ghominisl	:	ATGGGGAAA	CCTTCAAGC	CAGCAACGCCC	CGTGGAGG	:	364
Ghominis21	:	ATGGGGGGAA				:	365
Hfelis gb	:	AT GGG GGCAL				:	390
Hbizzozero	:	ATGGG GGCAA				:	365
Hsalomonis	:	ATGGGGGAA				:	322
Abutzleri	:	ATGGACGAAA				:	410
Cjejunilgb	:	ATGGC GAAA				:	406
Wsuccinoge	:	ATGGGGAAA				:	395
		ATGGg GaAA	CCTGAaG	CAGCAACGCCC	CGTGGAGG		

Figure 1 - 16

		600	*	620			
HbovisR2XA	:	ATGAAGGTTCTAGGAT	TGTAA	ACTOCTITE	GAGAC	:	398
Hpylori qb	:	ATCAAGGTTTTAGGAT	TGTAA	ACTOS:TIT	TAGAC	:	432
Hbilis qb	:	ATGAAGGTTTTAGGAT	TOTAA	ACTOSTITI:	AAGAC	:	602
Hcanis qb	:	ATGAAGGTTTTAGGAT	TOTAA	actocttt å	AAGAG	:	422
Hcinaedi q	:	ATGAAGGTTTTAGGAT	TGTAA	ACTCCKTTT	AAGAC	:	430
Hacinonych	:	ATCAAGGTTTTAGGAT	TOTAA	ACT COTTOT 3	CAGAC	:	431
Hnemestrin	:	ATGAAGGTTTTAGGAT	TGTAA	ACTCCTTTT (CAGAG	:	428
Hcholescys	:	ATGAAGGTTTTAGGAT	TOTAA	ACTECTITIS	GAGAG	:	412
Hpamatensi	:	ATGAAGGTTTTAGGAT	TGTAA	ACTCCTTTE賃	TAGAG	:	432
Hmustelae	:	ATGAAGGTTTTAGGAT	TGTAA	ACTECTTTTE	PAGAC	:	431
Hrodentium	:	ATGAAGGTTTTCGGAT	TGTAA	ACTCCTITIC	AAGAG	:	406
Hpullorum	:	ATGLAGGTTTTCGGAT	TOTAA	ACTCCTTTT[]	TAGAC	:	423
Hfennellia	:	ATGAAGGTTTTAGGAT	TUTAA	actconntt\{\}	TAGAG	:	431
Htrogontum	:	ATGAAGGTTTTAGGAT	TUTAA	ACTCCTTTTC	"AAGAC	:	408
Hmuridarum	:	ATGAAGGTTTTAGGAT	TGTAA	ACTCCTTT: 🗟	GAGAG	:	427
Hhepaticus	:	atgaaggtttaagat				:	407
Ghominisl	:	ATGAAGGTTT FAGGAT				:	401
Ghominis21	:	ATGAAGGTTTTAGGAT				:	402
Hfelis gb	:	ATGAAGGTTT TAGGAT				;	427
Hbizzozero	:	ATGAAGGTTTTAGGAT				:	402
Hsalomonis	:	ATGAAGGTTTTAGGAT				:	359
Abutzleri	:	ATGACACATTTCGCTC				:	447
Cjejunilgb	:	ATGACACTTTTCGGA				:	443
Wsuccinoge	:	ATGAAGGTCTTCGGAT				:	432
		ATGAaggtttTaGGat	tGTAA	ACTCCTTTT	T agaG		

Figure 1 - 17

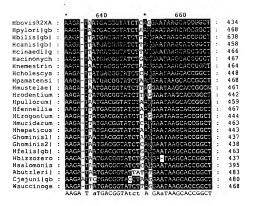


Figure 1 - 18

		*	680	*	700		
HbovisR2XA	:	AACTCCGTGC	CAGCAGCC	GCGGTAATAC	GGAGGGTGC	:	471
Hpylorilqb	:	AACTCCGTGC	CAGCAGCC	GCGGTAATAC	GGAGGGTGC	:	505
Hbilis(gb)	:	AACTCCGTGC	CAGCAGCC	GCGGTAATAC	GGAGGGTGC	:	675
Hcanislabl	:	AACTCCGTGC	CAGCAGCC	GCGGTAATAC	GGAGGGTGC	:	495
Hcinaedilg	:	AACTCCGTGC	CAGCAGCC	GCGGTAATAC	GGAGGGTGC	:	503
Hacinonych	:	MACIFICATION	CAGCAGCC	GCGGTAATAC	GGAGGGTGC	:	504
Hnemestrin	:	AACTCCGTGC	CAGCAGCC	GCGGTAATAC	GGAGGGTGC	:	501
Hcholescys	:	AACTCCGTG(CAGCAGCO	GCGGTAATAC	GGAGGGTGC	:	485
Hpamatensi	:	NACTOOGTGO				:	505
Hmustelae	:	NACTCCGTGC	CAGCAGCC	GCGGNANTAC	GGAGGGTGC	:	504
Hrodentium	:	AACTCCGTGC	CAGCAGCC	GCGGTAATAC	GGAGGGTGC	:	479
Hpullorum!	:	AACTCCGTGC				:	496
Hfennellia	:	AACTCCGTGC	CAGCAGC	GCGGTAATAC	GEAGGGTGC	:	504
Htrogontum	:			GCGGTAATAC		:	481
Hmuridarum	:	NACTICCGTGC	CAGCAGC	GCGGTAATAC		:	500
Hhepaticus	:	AACTCCGTGC			GGAGGGTGC	:	464
Ghominis1	:			GCGGTAATAC		:	474
Ghominis2	:	AACTCCGTG				;	475
Hfelis gb	:	ANCTCCGTGC				:	500
Hbizzozero	:			GCGGTAATAC		:	474
Hsalomonis	:			CGCGGTAATAC		:	432
Abutzleri	:			CGCGGTAATA		:	520
Cjejunilgb	:			GCGGTAATA		:	517
Wsuccinoge	:			CGCGGTAATA		:	505
		AACTCCGTG	CCagcago	cgcggtaata(CGGAGGGTGC		

Figure 1 - 19

			720	*	740		
HbovisR2XA	:	AAGCGTTACT	CGGAATCACIGG	GCGTAAAGA	G_{i} CTGT	:	508
Hpylorilgb	:	AAGCGTTACT	CEGAATCACTGG	GCGTAAAGA	GGCGT	:	542
Hbilis gb	:	AAGCGTTACT	COPARTURCTOS	GOGTAAAGA	CCCT	:	712
Hcanis gb	:	AAGCGTTACT	COGAATCACTGG	SOSTARAGA	CLGCGT	:	532
Hcinaedilg	:	AAGCGTTACT	COGRATCACTOR	RESTRANGA	GTGCGT	:	540
Hacinonych	:	AAGCGTTAUI	COGGARTCACT GO	GCGTAAAGA	GECGT	:	541
Hnemestrin	:	AAGCGTTACT	COGGRATUACING	GOGTAAAGA	G GCGT	:	538
Hcholescys	:	AAGCOTTACT	CGGAATCACTGG	GOGTAAAGA	G. GCGT	:	522
Hpamatensi	:	NAGCGTTACT	CGGAATCACTGG	GCGTAAAGA	CT GCGT	:	542
Hmustelael	:	NAGCGTTACT	CGGAATCACTGG	GCGTHAAGA	G'EGCGT	:	541
Hrodentium	:	AAGCGTTAC:	CGGAATCACTGG	GCGTAAAGA	GÜGCGT	:	516
Hpullorum!	:	AAGCGTTACT	CGGAATCACTGG	GCGTAAAGA	GMGCGT	:	533
Hfennellia	:	AAGCGTTAC	CCGGAATCACTGG	GCGTAAAGA	CTSCCC	:	541
Htrogontum	:		CGGAATCACTGG			:	518
Hmuridarum	:	AAGCGTTAC:	CGGAATCACTGG	GCGTAAAGA	CTESCC	:	537
Hhepaticus	:	AAGCGTTAC:	PCGGAATCACTGG	GCGTAAAGA	CT ECCT	:	501
Ghominis1	:		CGGAATCACTGG			:	511
Ghominis2	:		CGGAATCACTGG			:	512
Hfelis gb	:		reggaatenetgg			:	537
Hbizzozero	:		CGGAATCACTGG			:	511
Hsalomonis	:		CGGAATCACTGG			:	469
Abutzleri	:		reggaatcactgg			:	557
Cjejunilgb	:		CGGAATCACTGG			:	554
Wsuccinoge	:		reggaateaetgg			:	542
		AAGCGTTAC	rcggaatcactgg	GCGTAAAGa	G gcGt		

Figure 1 - 20

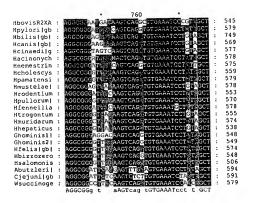


Figure 1 - 21

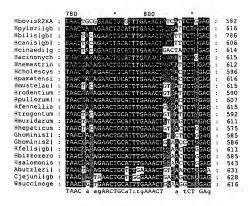


Figure 1 - 22

		820	*	840			
HbovisR2XA	:	TFTGGGAGAGG	AGGTGGAA	CTTGGTGTA	AGGGGTA	:	619
Hpylorilgb	:	TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	PAGGTGUAAS	FICTTSGTGT!	AUGGGTA	:	653
Hbilis gb	:	TATEGUAGAGE	TAUGTGGAAT	PTOTTUGTGTA	AGGGGTA	:	823
Hcanis gb	:	TATGGGAGAGG	PAGGTCBAAN	rrettagtata	AGGGGTA	:	643
Hcinaedilg	:	TATECCAGAGO	PAGGTGGAA	POTTGGTGF	GGGGTA	:	651
Hacinonych	:	TFTGGGAGAGGG	YAGGTGGAAT	TOTTOGTGT	AGGGGTA	:	652
Hnemestrin	:	TATGGGAGAGG	PAGGTGJAA:	TOTTUGTGT/	CAGGTA	:	649
Hcholescys	:	TATEGGAGAGG	TAGGTGGAAT	TCTTGGTGT:	AGGGGTA	:	633
Hpamatensi	:	TATGGGAGAGG	TAGGTGGAAT	PROTTGGTGT	AGGGGTA	:	653
Hmustelael	:	TET GGGAGAGC	TAGGTGGAA!	PICTTGGTGT	GGGGTH	:	652
Hrodentium	:	TATGGGAGAGG'	TAGGIGGAA	PTCTTGGTGT.	AGGGGTA	:	627
Hpullorum	:	TATGGGAGAGG	TAGGT GGAA'	PICTTOSTOT.	AGGGGTA	:	644
Hfennellia	:	TSTEGGAGAGG				:	652
Htrogontum	:	TETEGGAGAGG	TAGGIGGAX	PTCTTGGTGT.	AGGGGTA	:	629
Hmuridarum	:	TETGGGAGAGG				:	648
Hhepaticus	:	TATGGGAGAGG				:	612
Ghominis1	:	TETEGGAGAGG				:	622
Ghominis2	:	THTGGGAGAGG	Tag g tggah	FTCTFGGTGT.	AGGGGTA	:	623
Hfelis gb 	:			PTCTTGGTGT.		;	648
Hbizzozero	:	TETGGGAGAGG				:	622
Hsalomonis	:			TTCTTGGTGT.		:	580
Abutzleri	:	TATEGGAGAGG				:	668
Cjejuni gb	:	TEAGGGAGAGG				:	665
Wsuccinoge	:			TTCTCGGTGT		:	653
		T tGGGAGAGG	LAGGTGGAA	tTcttGGTGT	AGGGGTA		

Figure 1 - 23

		860 * 880		
HbovisR2XA	:	AAATCCUTAGATATCAAGAMGAATACTCATTGCGAAG	:	656
Hpylorilqb	:	AAATCCCTAGAGAICAAGAGGAATACTCATTGCGAAG	:	690
Hbilis qb	:	AAATCCCTAGAGATCAAGAGGAATACTCATTGCGAAG	:	860
Hcanisighi	:	AAATCOUTAGAGATCAAGAGGAATACTCATTGCGAAG	:	680
Hcinaedilg	:	AAATCCCTAGAGATCAAGAGGAATACTCATTGCGAAG	:	688
Hacinonych	:	AAATCCCTAGAGATCAAGAGAATACTCATTGCGAAG	:	689
Hnemestrin	:	AAATUOGTROAGATOARGAGGAFTACTCATTGCGAAG	:	686
Hcholescys	:	AAATCUU <mark>C</mark> AGAGATCRAGAGGAATACTCATTGCGAAG	:	670
Hpamatensi	:	AAATCCGTAGAGATCAAGAGGAATACTCATIGCGAAG	:	690
Hmustelael	:	AAATCCGTAGAGATCAAGAGGAATACTCATTGCGAAG	:	689
Hrodentium	:	AAATCCGTAGAGATCAAGAGSAATACTCATTGCGAAG	:	664
Hpullorum	:	AAATCCGTAGAGATCAAGAGGAATACTCATTGCGAAG	:	681
Hfennellia	:	AAATCCGTAGAGATCAAGAGGAATACTCATTGCGAAG	:	689
Htrogontum	:	AAATCCGTAGAGATCAAGAGGAATACTCATTGCGAAG	:	666
Hmuridarum	:	AAATCCGTAGAGATCAAGAGGAATACTCATTGCGAAG	:	685
Hhepaticus	:	AAATCCGTAGAGATCAAGAGGAATACTCATTGCGAAC	:	649
Ghominis1	:	AAATCCGTAGAGATCAAGAGGAATACTCATTGCGAAG	:	659
Ghominis2	:	AAATCCGTAGAGATCAAGAGGAATACTCATTGCGAAC	:	660
Hfelis gb	:	AAATCCGTAGAGATCAAGAGGAATACTCATTGCGAAG	:	685
Hbizzozero	:	AAATCCGTAGAGATCAAGAGGAATACTCATTGCGAAG	:	659
Hsalomonis	:	AAATCCGTAGAGATCAAGAGGAATACTCATTGCGAAG	:	617
Abutzleri	:	AAATCCGTAGAGATCAGAAGGAATACCGATTGCGAAG	:	705
Cjejuni gb	:	AAATCCGTAGA <mark>T</mark> ATCA <mark>CC</mark> AAGAATACCCATTGCGAAC	:	702
Wsuccinoge	:	AAATCCGTAGAGATC <mark>G</mark> AGAGGAATACTCATTGCGAAC	:	690
		AAATCCGtAGAGATCaagAgGAATACtcATTGCGAAG		

Figure 1 - 24

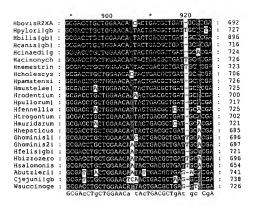


Figure 1 - 25

		*	940	*	960		
HbovisR2XA	:	AAGCGTGGG	GAGCAAACAG	GATTAGATA	CCCTGGTAG	:	729
Hpylorilab	:	AAGCGTCGC	GAGCAAACAG	GATTAGATA ²	COCTGGTAG	:	764
Hbilislabl		AAGCGTGGG	GAGCAAACAG	GATTAGATA:	CCTGGTAG	:	933
Hcanislabl	:	AAGC=TOOC	COAGCANACEC	GATTAGAJA	CCCTGGTAG	:	752
Heinaedilg		AAGCGTGG	GAGCARACAG	GATTAGATA	CCCTGGTAC	:	761
Hacinonych	;		GCAGCAAACAG			:	763
Hnemestrin		AAJCGTGGG	ggaggaaAAcAC	CATTAGATA	CCCTGGTAG	;	760
Hcholescys	į.		GGAGCAAACAC			:	743
Hpamatensi	:		GGAGCAAACAC			:	763
Hmustelaei	9		GGAGCAAACAC			:	762
Hrodentium	:	AAGCGTGG	GGAGCAAACAC	GATTAGATA	CCCTGGTAG	:	737
Hpullorumi			GGAGCAAACAC			:	753
Hfennellia	:		GGAGCAAACAC			:	762
Htrogontum	:	AAGCGTGG	GGAGCAAACAC	GATTAGATA	CCCTGGTAG	:	739
Hmuridarum	:	AAGCGTGG	GGAGCAAACAC	GATTAGATA	CCCTGGTAC	:	758
Hhepaticus	:	AAGCGTGG	GGAGCAAACAC	GATTAGATA	CCCTGGTAG	:	722
Ghominis1	:	AAGCGTGG	GGAGNAAACAG	GATTAGATA	CCCYGGTAG	:	733
Ghominis21	:	AAGCGTGG	GGAGCAAACAC	GATTACATA	CCCTGGTAG	:	734
Hfelis gb	:		GGAGCAAACAG			:	758
Hbizzozero	:		GGAGCAAACAG			:	733
Hsalomonis	:		GGAGCAAACA(691
Abutzleril	:		GGAGCAAACAG				778
Cjejunilgb	:		GGAGCAAACA				775
Wsuccinoge	:		GGAGCAAACA				763
		AAGCATGG	GGAGCAAACAI	CATTAGATA	CCCTGGTAG		

Figure 1 - 26

			980	*	100		
HbovisR2XA		TOCACGCCCTAA.	CGATGGETG	OTTANTED OF	GGGG	:	766
Hpylorijgb		TOCACGCCCTAA				:	801
Hbilis qb		TOCACCOCCTAA				:	970
Heanisighi		TCCACGCCTAA.				:	789
Hcinaedilg	:	TOCACGUCCTAA				:	798
Hacinonych	:	TOCACGCCCTAA				:	800
Hnemestrin		TOCACGCCCTAA				:	797
Hcholescys	:	TOCACGCCCTAA				:	780
Hpamatensi	:	TCCACGCCCTAA				:	800
Hmustelael		TCCACGCCCTAA				:	799
Hrodentium	:	TCCACGCCCTAA				:	774
Hpullorum		TCCACGCCCTAA				:	790
Hfennellia		TCCACGCCCTAA				:	799
Htrogontum	:	TOCACGCCCTAA				:	776
Hmuridarum		TCCACGCCCTAA				:	795
Hhepaticus	:	TCCACGCCCTAA	ACGATGGATC	SCTAGTTGTTG	CCTT	:	759
Ghominisli	:	TOCACGOCCTAA	ACGATOGATO	SCTAGITGITC	G-AGC	:	769
Ghominis2	:	TCCACGCCCTAA	ACGATE <mark>G</mark> ATO	SCHAGTIGITS	GGGGG	:	771
Hfelis gb	:	TCCACGCCCTAA	ACGATGGAT(GCTAGTTGTTG	GGGGG	:	795
Hbizzozero	:	TCCACGCCCTAA				:	770
Hsalomonis	:	TCCACGCCCTAA				:	728
Abutzleril	:	TCCACGCCCTAA				:	815
Cjejunilgb	:	TCCACGCCCTNA	ACGATOTAC	ACTAGTTGTTC	GGGTG	:	812
Wsuccinoge	:	TCCACGCCCTAA				:	800
		TCCACGCCCTAA	ACGATG At	gCTAgTTGTtC	G		

Figure 1 - 27

		0		1020			
HbovisR2XA			TCCT		TAACGCHTTAAGCA		802
Hpylorijgb	:				TARCGONTTAAGCA		838
Hbilis qb	:				TAACGCMYTAAGCA		1006
Hcanis qb	;				TAACGUÜTTAAGCA	ı,	825
Hcinaedilg	:				TAACGCWTTAAGCA	ı.	834
Hacinonych	:				TAACG. CTTAAGCA	ď.	837
Hnemestrin	:				TAACGUETTAAGCA	i.	834
Hcholescys	:				AACGC TTAAGCA		816
	:				TAACGCOTTAAGCA	:	836
Hpamatensi	-				TAACACATTAAGCA	1	835
Hmustelae Hrodentium	:				TAACGCHTTAAGCA	1	810
	:					٠.	826
Hpullorum	:				TAACGC TTAAGCA	:	
Hfennellia	:				TAACGC TTAAGCA	:	835
Htrogontum	:				TAACGCHTTAAGCA	:	812
Hmuridarum	:				TAACGCATTAAGCA	:	831
Hhepaticus	:				TAACGCETTAACCA	:	795
Ghominis1	:				TAACGCCTTAAHNA		806
Ghominis2	:				TAACGC <mark>C</mark> TTAAGCA		808
Hfelis gb	:				TAACGC <mark>C</mark> TTAACCA		831
Hbizzozero	:				TAACGC <mark>C</mark> TTAAGCA		807
Hsalomonis	:				TAACGCCTTAAGCA		765
Abutzleri	:				TAACACATTAAGTG		851
Cjejunilgb	:				TAACGCATTAAGTG		848
Wsuccinoge	:	CTT-S	TCAGGGC	AGTAATGCAGI	TAACACUTTAAGCA	:	836
		CTt G	tC C	aGTAATGCAgo	TAACGC TTAAGC		

Figure 1 - 28

		1040	*	1060			
HbovisR2XA	:	1 CCCGCCTG	GGGAGTACG	ATCGCAAGA	TAAAACTCA	:	839
Hpylorilgb	:	TOCCUCCTO	GGGAGTACC	GTOGCAAGA"	FTAAAACTCA	:	875
Hbilis gb	:	TECCGCCTG	GUGAGTACS	GTCGCRAGA"	TAAAAACTCA	:	1043
HcanisIgbl	:	IT CCCCCTG	GGGAGTACC	GTCGCAAGA1	TTAAAACTCA	:	862
Hcinaedilg	:	TACCCCCTG	GGGAGTACG	GTCGCAAGA!	TAAAACTCA	:	871
Hacinonych	:	recedente	GGGAGTACE	GTCGCAAGA	FFAAAACTCA	:	874
Hnemestrin	:	TOCCCCCTO	GGGAGTACS	GTOGCAAGA"	PTAAAACTCA	:	871
Hcholescys	:	TROCGCCTG	GGGAGTACG	GTCGCAAGA"	FTAAAACTCA	:	853
Hpamatensi	:	TECCCCTC	GGGAGTACG	GTCGCAAGA1	FFAAAAC FCA	:	873
Hmustelae	:	TROCGCCTG	GGGAGTACG	GTCGCAAGA*	FTAAAACTCA	:	872
Hrodentium	:	TECCCCCTG	GGGAGTACG	GTCGCAAGA	FTAAAACTCA	:	847
Hpullorum!	:	TECCCCTC	GGGAGTACG	GTCGCAAGA"	TTAAAACTCA	:	863
Hfennellia	:	TTCCCCCTC	GGGAGTACG	GTCGCAAGA'	TTAAAACTCA	:	872
Htrogontum	:	TECCCCCTC	GGGAGTACG	GTCGCAAGA*	TARABOTOR	:	849
Hmuridarum	:	TTCCCCCTG	GGGAGTACG	GTCGCAAGA'	TTAAAACTCA	:	868
Hhepaticus	:	TOCCCCCTG	GGGAGTACG	GTCGCAAGA	FTAAAACTCA	:	832
Ghominisl	:	TCC-SCCTS	GGGAGTACG	GTCGCAAGA"	TTAAAACTCA	:	842
Ghominis2)	:				TTAAAACTCA	:	845
Hfelis gb	:				PTAAAACTCA	:	868
Hbizzozero	:				PTAAAACTCA	:	844
Hsalomonis	:				TTAAAACTCA	:	802
Abutzleri	:				TTAAAACTCA	:	888
Cjejunilgb	:				ITAAAACTCA	:	885
Wsuccinoge	:				TTAAAACTCA	:	873
		T CCGCCTG	GGGAGTACC	gTCGCAAGA	TTAAAACTCA		

Figure 1 - 29

		1080		1100	*		
HbovisR2XA	:	AAGGAATAGA	CGGGGGACTC	GCACAAGCGGT:	GGAGCAT	:	876
Hovlorilab	:	AAGGAATAGA	CGGGGGACCC	GCACAAGCGGT	GUAGCAN	:	912
Hbilis qb				BCACAAGC3GT		:	1080
Hcanislabl	:			GCACAAGCGST		:	899
Heinaedilg	:			CONCACACCOCT		:	908
Hacinonych				GCACAAGCGGT		:	911
Hnemestrin	:			GCACAAGCGGT		:	908
Hcholescys	:			GCACAAGCGGT		:	890
Hpamatensi				GCACAAGCGGT		:	910
Hmustelael				GCACAAGCGGT		:	909
Hrodentium	:			GCACAAGCGGT		:	884
Hpullorum	:	AAGGAATAGA	CGGGGACCC	GCACAAGCGGT	GGAGCAT	:	900
Hfennellia	;	AAGGAATAG/	CGGGGACCC	GCACAAGCGGT	GGAGCAT	:	909
Htrogontum	:	AAGGAATAGA	CGGGGACCC	GCACAAGCGGT	GGAGCAT	:	886
Hmuridarum	:	AAGGAATAGA	CGGGGACCC	GCACAAGCGGT	GGAGNNE	:	905
Hhepaticus	:	AAGGAATAGA	CGGGGACCC	GCACAAGCGGT	GGAGCAT	:	869
Ghominis1	:	AAGGAATAGA	CCCCCACC-	GCACAAGCGGT	GCAGCAT	:	878
Ghominis2	:	AAGGAATAGA	CGGGGACCC	GCACAAGCGGT	GGAGCAT	:	882
Hfelis gb	:			GCACAAGCNRX		:	905
Hbizzozero	:			GCACAAGCGG"		:	881
Hsalomonis	:			GCACAAGCGGT		:	839
Abutzleri	:			GCACAAGCGG1		:	925
Cjejunilgb	:			GCACAAGCGGT		:	922
Wsuccinoge	:			GCACAAGCGGT		:	910
		AAGGAATAGA	ACGGGGACCC	:GCACAAGCGG1	GGAGCAT		

Figure 1 - 30

		1120 * 1140		
HbovisR2XA	:	GTGGTTTARTTCGAAGATAC CCGAAGAACCTTACCCA	:	913
Hpylorilgb	:	GTGGTTTRAT PCGAMMMACACGAAGAACCTTACCTA	:	949
Hbilislabl		GTGSTTTAATTCGAAGATACTCGAAGAACCTTACCTA	:	1117
Hoanistabl		GTGGTTTAAHTCGAAGATACLIGGAAGAACCTTACCTA	:	936
Hcinaedilg		GTGGTTTAATTCGAGTAYACKCGAAGRACCTTACCTA	:	945
Hacinonych		GTGGTTTAATTCGANHNNNCAUGAAGAACCTTAGCTA	:	948
Hnemestrin		GTUGTTTAATTCGAAGGTAC ROGARGARCOTTACCTA	:	945
Hcholescys		GTGGTTTAATTUGAAGATACLCGAAGAACCTTACCTA	:	927
Hpamatensi	:	GTGGTTTAATTCGANNHTACHCGAAGAACCTTACCTA	:	947
Hmustelael		GTGGTTTAATTCGANHNTACCCGAAGAACCTTACCTA	:	946
Hrodentium	:	STGGTTTAATTCGAASATACACGAAGAACCTTACCTA	:	921
Hpullorum	:	GTGGTTTAATTCGAAGATACTCGAAGAACCTTACCTA	:	937
Hfennellia	:	GTGGTTTAATTCGAANNTAC%CGAAGAACCTTACCTA	:	946
Htrogontum	:	GTGGTTTAATTCGAAGATAC GGAAGAACCTTACCTA	:	923
Hmuridarum	:	GTGGTTTAATTCGANHNNAC GGAAGAACCTTACCTA	:	942
Hhepaticus	:	GTGGTTTAATTCGAAGATAC@CGAAGAACCTTACCTA	:	906
Ghominisl	:	GTGGTTTAATTCGAAGATACACGAAGAACCTTACCTF	:	915
Ghominis2	:	GTGGTTTAATTCGAAGATACACGAAGAACCTTACCTA	:	919
Hfelis gb	:	GTGGTTTAATTCGANNNNNNMCGAAGAACCTTACCTA	:	942
Hbizzozero	:	GTGGTTTAAT FCGAAGATACACGAAGAACCTTACCTA		918
Hsalomonis	:	GTGGTTTAATTCGA <mark>T</mark> GCTAC <mark>A</mark> CGAAGAACCTTACCTA		876
Abutzleri	:	GTGGTTTAATTCGANNNACACGAAGAACCTTACCTG		962
Cjejunilgb	:	GTGGTTTAATTCGAAGNTAC CGAAGAACCTTACCTG		959
Wsuccinoge	:	GTGGTTTAATTCGANNNNAC∰CGAAGAACCTTACCTG		947
		GTGGTTTAATTCGAagaTAC CGAAGAACCTTACCta		

Figure 1 - 31

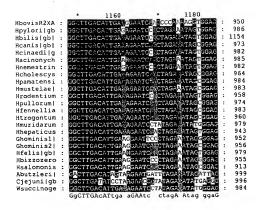


Figure 1 - 32



Figure 1 - 33

		*	1240		12			
HbovisR2XA	:	GGUTGTCGTC	AGCTCGTGTCG	TGAGATGTT	GGGTTAA	:	1023	
Hpylorilgb	:	GGCTGTCGTC	AGCTCGTGTCG	TGAGATGIT	GGGTTAR	:	1060	
Hbilis qb	:	GGCTGTCGTC	AGCTCGTGTCG	TGAGATGTT	GGGTTAA	:	1227	
Hcanis gb	:	GGCIGTCGTU	ASCIOCICIO	TGAGATGTT	GGGTTAA	:	1047	
Hcinaedilg	:	GGCTGTCGTC	AGCTOSTOICO	TGAGATGTT	GGGTTAA	:	1055	
Hacinonych	:		ASSTORTATOR			:	1059	
Hnemestrin	:	GGCTCTCGTC	ASSIGNATION	TO/CATGIT	GGSTTAL	:	1056	
Hcholescys	:		AGCTCGTGTCC			:	1037	
Hpamatensi	:	EGCTGTCGTC	AGCTCGTGTCC	TOAGATGTT	GGGTTAA	:	1057	
Hmustelae	:	GGCTGTCGTC	AGCTCCTGTCC	TGAGATGTI	GGGTTAA	:	1057	
Hrodentium	:	GGCTGTCGTC	AGCTCGTGTCC	TGAGATGTT	GGGTTAA	:	1031	
Hpullorumi	:	GCCTCTCGTC	CAGCTCCTGTCC	TGAGATGTT	GGGTTAA	:	1047	
Hfennellia	:	GGCTGTCGTC	AGCTCGTGTCC	TGAGATGTT	GGGTTAA	:	1056	
Htrogontum	:		AGCTCGTGTCC			:	1031	
Hmuridarum	:	GGCTGTCGTC	CAGCTCGTGTCC	STGAGATGT'I	GGGTINA	:	1052	
Hhepaticus	:		AGCTCGTGTCC			:	1013	
Ghominis1	:		:AGCTCGTGTCC			:	1026	
Ghominis2	:		AGCTCGTGTCC			:	1030	
Hfelis gb	:		CAGCTCGTGTCC			:	1053	
Hbizzozero	:		CAGCTCGTGTCC				1029	
Hsalomonis	:		CAGCTCGTGTCC				987	4
Abutzleri	:		CAGCTCGTGTC				1072	
Cjejuni gb	:		CAGCTCGTGTC				1069	
Wsuccinoge	:		CACCTCGTGTC				1057	
		GGCTGTCGT	CAGCTCGTGTC	STGAgATGT'	rgggttaa			

Figure 1 -34

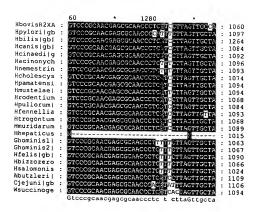


Figure 1 - 35

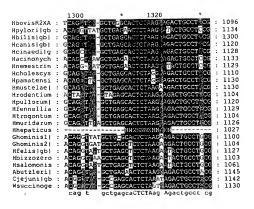


Figure 1 - 36



Figure 1 - 37

			1380		140	00		
HbovisR2XA	:	TEGCCCT	TETET SO	GGGCTAC	GCACGTG	CTACAATO	:	1170
Hpylori qb	:	TEGCCCT	TACGCC	AGGGCTAC	ACACGTG	CTACARTO	:	1208
Hbilis qb	:	TEGECET	TACGCCT	AGGGCTAC	ACACGTG	CTACAATG	:	1374
Hcanis qb	:			AGGGCTAC			:	1194
Hcinaedilg	:	TEGCCCT	TACGCCT	AGGGCTAC	ACACGIG	CTACAATG	:	1202
Hacinonych	:	TEGCCCT	TACGCCT	AGGGCTAC	ACACGTG:	CTACAATO	:	1207
Hnemestrin	:	TEGECECT	TACGCCI	AGGGCTAC	ACACGTG:	CTACAATG	:	1203
Hcholescys	:	TGGCCCT	TACGCCI	AGGGCTAC	ACACGTG:	CTACAATG	:	1184
Hpamatensi	:	TGGCCCT	TACGCCT	AGGECTAC	ACACGTG	CTACAATG	:	1204
Hmustelae	:	TGGCCCT	T#CGCC1	PAGGGCTAC	ACACGTG:	CTACAATG	:	1204
Hrodentium	:	TEGECCET	TACGCCT	PAGGGCTAC	ACACGTG	CTACAATG	:	1178
Hpullorum	:	TGGCCCT	TACGCCI	FAGGGCTAC	ACACGTG	CTACAATC	:	1194
Hfennellia	:	TESCCCT	TACGCC!	PAGGGCTAC	ACACGTG	CTACAATC	:	1203
Htrogontum	:	TGGCCCT	TACGCC'	PAGGGCTAC	ACACGTG	CTACAATC	:	1178
Hmuridarum	:	TEGCCCT	TACGCC!	PAGGGCTAC	ACACGTG	CTACAATG	:	1200
Hhepaticus	:						:	1057
Ghominis1	:			PAGGGCTAC			:	1170
Ghominis2	:			PAGGGCTAC				1178
Hfelis gb	:			PAGGECTAC				1201
Hbizzozero	:			[AGGGCTAC				1177
Hsalomonis	:			<u>r</u> agggctac				1135
Abutzleri	:			CAGGGCTAC				1219
Cjejunilgb	:			AGGGCGAC				1216
Wsuccinoge	:			YAGGGCTAC				1204
		tggccct	tAcgcc	tagggctad	acacgtg	ctacaATG		

Figure 1 - 38

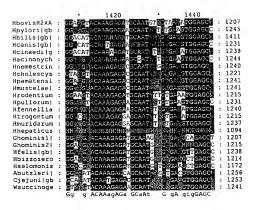


Figure 1 - 39

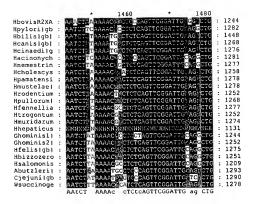


Figure 1 - 40

			1500	*	1	
HbovisR2XA	:	CAACTOGROOMCA	rgaagdaggaa	TCGCTAGTAATC		1281
Hpylorijab	:	CAACTCCOCTOCA	"GAAGCTGGAA	TOGOTAGTAATO	: 6	1319
Hbilislabl	:	CAACTOO! CT ICA	AAAGCTGGAA	ATCOCTAGTAATC	9 :	1485
Hcanis gb	:	CAACTCG/CT CA	I GAAUCTGGAA	ATCECTAGTAATO	:	1305
Hcinaedilg	:	CAACTOO! CT*CA	TARACCTAGAS	ATOGOTAGTAATO	9 :	1313
Hacinonych	:	CAACTOGGCTGCA	TGAAGC G UGAA	AFOGCTAGTAATO	3 :	1318
Hnemestrin	:	CAACTCGCCTGCA	TGAAGOTGGAA	STOCUTACTARTO	G :	1314
Hcholescys	:	CANCITUCACTACA	TGAAGCTGGA/	NTOGOTAGTAATO	3 :	1295
Hpamatensi	:	CAACTCG CT CA				1315
Hmustelael	:	CAACTCO CT CA	TGAAGCTGGAA	RTCGCTAGTAATC	G :	1315
Hrodentium	:	CAACTCGNCTGCA	TGAAGCTGGA:	TCGCTAGTAATC	G :	1289
Hpullorum	:	CAACTCGACT CA	TGAAGCTGGA;	ATCGCTAGTAATC	G :	1305
Hfennellia	:	CAACTCCCCTCA	TAAASCTGGA:	ATCCCTACTAATC	e :	1314
Htrogontum	:	CAACTCGACTACA				1289
Hmuridarum	:	CAACTCG/CT CA	TGAAGCTGGAA	ATCGCTAGTAATC	3 ∶	1311
Hhepaticus	:	NNNHWHNESHNENK				1168
Ghominisl	:	CAACTCGCCTGCA	TGAAGCTGGA	ATCGCTAGTAATC	G :	1281
Ghominis2	:	CAACTCGCCTGCA				1289
Hfelis gb	:	CAACTCCCCTGCA				1312
Hbizzozero	:	CAACTCGCTCCA				1288
Hsalomonis	:	CAACTOGCCTGCA				1246
Abutzleri	:	CAACTCGCCTACA				
Cjejunilgb	:	CAACTCG GAGCA				
Wsuccinoge	:	CAACTCGCCTCCA				1315
		CAACTCG Ct CA	TgAAGctGGA.	ATCGCTAGTAATC	G	

Figure 1 - 41

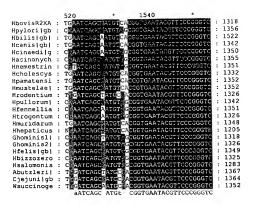


Figure 1 - 42



Figure 1 - 43

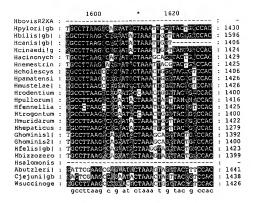


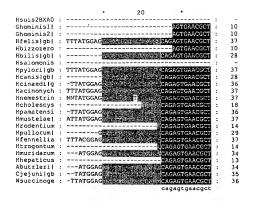
Figure 1 - 44

		*	1640	*	1660		
HbovisR2XA	:					:	-
Hpylorilgb	:	SGC ACAC	ACAGCGACTGGG			:	1450
Hbilis gb	:	GC A	GCAGCGACTGGG			:	1616
Hcanisigbi	:					:	-
Hcinaedilg	:		GCAGCGACTGGG:			:	1444
Hacinonych	:	GCACAC	ACAGCGACTGGG			:	1449
Hnemestrin	:	CCCAC	ACAGCGACTGGG			:	1462
Hcholescys	:	GC TAI	GCAGCGACTGGG-			:	1425
Hpamatensi	:	GC AI	GOAGCGACTGGG			:	1446
Hmustelae	:		NO			:	1435
Hrodentium	:		GCAGCGACTGGG			:	1423
Hpullorum	:	《GC 特AI				:	1428
Hfennellia	:		GCAGCGACTGGG			:	1445
Htrogontum	:		GCAGCGACTGCG			:	1422
Hmuridarum	:		GCAGCGACTGGG			:	1442
Hhepaticus	:		GCAGCGACTGGG:			:	1302
Ghominis1	:		ACAGCGACTGGG;			:	1414
Ghominis2	:		ACAGCGACTGGG			:	1422
Hfelis gb	:		ACAGCGACTGGG			:	1443
Hbizzozero	:	BECACE C	ACAGCGACTGGG			:	1421
Hsalomonis	:					:	
Abutzleril	:		TCAGYGACTGGG			:	1461
Cjejunilgb	:		TCAGCGACTGGG			:	1458
Wsuccinoge	:		CAGCGACTGGG			:	1446

Figure 1 - 45

HbovisR2XA	:	:	-
Hpyloriigb	:	:	-
Hbilis gb	:	:	-
Hcanisighi	:	:	-
Hcinaedilg	:	:	-
Hacinonych	:	:	-
Hnemestrin	:	A :	1463
Hcholescys	:	:	-
Hpamatensi	:	:	-
Hmustelae	:	:	-
Hrodentium	:	:	-
Hpullorum!	:	;	-
Hfennellia	:	:	-
Htrogontum	:	:	-
Hmuridarum	:	;	-
Hhepaticus	:	:	
Ghominis1	:	:	-
Ghominis2	:	:	-
Hfelis gb	:	:	-
Hbizzozero	:	:	-
Hsalomonis	:	:	-
Abutzleri	:	:	-
Cjejunilgb	:	:	-
Wsuccinoge			_

Figure 1 ~ 46



		40	*	60				
Hsuis2BXA0	:			TGCAAGT	CGAACGA"	FGAAG	:	19
Ghominis1	:	GGCGGCGT	GCCTAATA	CATGCAAGT	CGAACGA"	rgaag	:	41
Ghominis21	:	GGCGGCGT	GCCTAATA	CATGCAAGT	CGAACGA"	'GAAG	:	41
Hfelis qb	:	GCCGCCGT	GCCTAATA	CATGCAAGT	CGAACGAS	rgaag	:	7.
Hbizzozero	:	GGCGGCGT	GCCTAATA	CATGCAAGT	CGAACGA	FGAAG	:	4
Hbilis qb	:	GGCGGCGT	GCCTAATA	CATGCAAGT	CGAACGA"	rgaag	:	65
Hsalomonis	:					GAAG	:	
Hpylorilgb	:	GGCGGCGT	GCCTAATA	CATGCAAGT	CGAACGA'	FGAAG	:	7
Hcanis qb	:	GGCGGCGT	GCCTAATA	CATGOMAGT	CGAACGA'	FGAAG	:	6
Hcinaedilg	:	GGCGGCGT	GCCTAATA	CATGCAAGT	CGAACGA'	FGAAG	:	7
Hacinonych	:			CATGCAAGT			:	7
Hnemestrin	:	GGCGGCGT	GCCTAATA	CATGCAAGT	CGAACGA'	TGAAA	:	7
Hcholescys	:	GGCGGCGT	GCCTAATA	CATGCAAGT	CGAACGA'	TGAAG	:	5
Hpamatensi	:	GGCGGCGT	GCCTAATA	CATCCAAGT	CGNACGA'	IGAAG	:	7
Hmustelae	:	GGCGGCST	GCCTAATA	CATGCAAGT	CGAACGA'	TGAAG	:	7
Hrodentium	:	GGCGGCGT	GCCTAATA	CATGCAAGT	CGAACGA'	TGAAG	:	5
Hpullorum	:	GCCGGCGT	GCCTAATA	CATGCAAGT	CGAACGA"	TGAAG	:	6
Hfennellia	:	GGCGGCGT	GCCTAATA	CATGCAAGT	CG4ACGA	TGAAC	:	7
Htrogontum	:	GGCGGCGT	GCCTAATA	CATGCAAGT	CGBACGA'	TGAAG	:	5
Hmuridarum	:	GGCGGCGT	GCCTAATA	CATGCAAGT	CGNACGA'	TGAAG	:	7
Hhepaticus	:			CATGCAAGT			:	5
Abutzleri	:	GGCGGCGT	GCTTAACA	CATGCAAGT	CGAACGA	GAACC	:	7
Cjejunilgb	:	GGCGGCGI	GCCTAATA	CATGCAAGT	CGNACGA	TGAAG	:	7
Wsuccinoge	:	GGCGGCGT	GCCTAATA	CATGCAAGT	CGAACGG	AACA	:	7
		ggcggcgt	gcctaata	catgcaagt	cgaacga	tqAaq		

Figure 2 -2

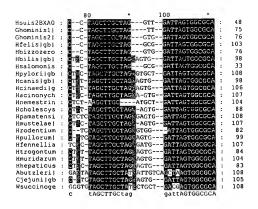


Figure 2 - 3

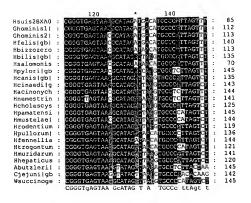


Figure 2 - 4

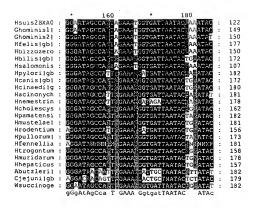


Figure 2 - 5

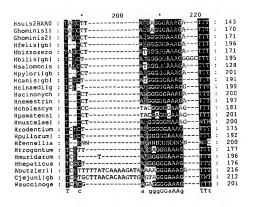


Figure 2 - 6

			*	240	*	26		
Hsuis2BXA0	:						:	-
Ghominisl	:						:	-
Ghominis2	:						:	-
Hfelis gb	:						:	-
Hbizzozero	:						:	-
Hbilis gb	:	CAATAAA	GAATTTC	TCTTTTTAC	STGCTTTGT	STTGTT	:	232
Hsalomonis	:						:	-
Hpylori gb	:						:	-
Hcanisigbl	:						:	-
Hcinaedilg	:						:	-
Hacinonych	:						:	-
Hnemestrín	:						;	-
Hcholescys	:						:	-
Hpamatensi	:						:	-
Hmustelael	:						:	-
Hrodentium	:						:	-
Hpullorum;	:						:	-
Hfennellia	:						:	-
Htrogontum	:						:	-
Hmuridarum	:						:	-
Hhepaticus	:						:	-
Abutzleri	:						:	-
Cjejunilgb	:						:	-
Wsuccinoge	:						:	-

		0	*	280	*		
Hsuis2BXA0	:					:	-
Ghominisl	:					:	-
Ghominis2	:					:	-
Hfelis gb	:					:	-
Hbizzozero	:					:	-
Hbilis qb	:	GGCACAAA	ATTCTAC	STATTTGGAAT	GAGAAATTGATG	:	269
Hsalomonis	:					:	-
Hpylorilgb	:					:	-
Hcanis gb	:					:	-
Hcinaedilg	:					:	-
Hacinonych	:					:	-
Hnemestrin	:	,				:	-
Hcholescys	:					:	-
Hpamatensi	:					:	-
Hmustelael	:					:	_
Hrodentium	:					:	-
Hpullorum	:					:	-
Hfennellia	:					:	-
Htrogontum	:					:	-
Hmuridarum	:					:	-
Hhepaticus	:					:	-
Abutzleri	:					:	-
Cjejunilgb	:					:	-
Wsuccinoge	:					:	-

		300	*		320	*		
Hsuis2BXA0	:						. :	-
Ghominis1	:						. :	-
Ghominis2	:						٠:	-
Hfelis qb	:						- :	-
Hbizzozero	:						- :	-
Hbilis qb	:	TTGTGAAGC	AATTTG'	TGCGG	AGACTAG	ACTTAGTGTC	: :	306
Hsalomonis	:						- :	-
Hpylori qb	:						- :	-
Hcanis qb	:						- :	-
Hcinaedilq	:						- :	-
Hacinonych	:						- :	-
Hnemestrin	:						- :	-
Hcholescys	:						- :	-
Hpamatensi	:						- :	-
Hmustelael	:						- :	-
Hrodentium	:						- :	-
Hpullorum	:						- :	-
Hfennellia	:						- :	-
Htrogontum	:						- :	-
Hmuridarum	:						- :	-
Hhepaticus	:						- :	-
Abutzleri	:						- :	-
Cjejunilgb	:						- :	-
Wsuccinoge	:						- :	-

		340		360	*		
Hsuis2BXA0	:					:	-
Ghominis1	:					:	-
Ghominis2	:					:	-
Hfelis qb	:					:	-
Hbizzozero	:					:	-
Hbilis qb	:	TGTCGCACAAGCA	AAATTGCG.	AACTCATCGATT	TATCG	:	343
Hsalomonis						:	_
Hpylorilgb							-
Hcanis qb	:					:	-
Hcinaedila	:						_
Hacinonych						:	-
Hnemestrin							-
Hcholescys						:	_
Hoamatensi	:						_
Hmustelael						÷	_
Hrodentium							_
Houllorum	:					:	_
Hfennellia						:	_
Htrogontum	:					:	_
Hmuridarum	:					:	-
Hhepaticus	:		<u>-</u>				-
Abutzleri	:					:	_
Cjejunilgb	:					:	_
Wsuccinoge	:					:	_

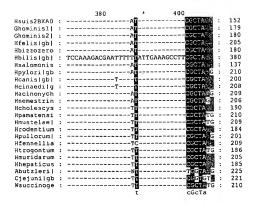


Figure 2 - 11

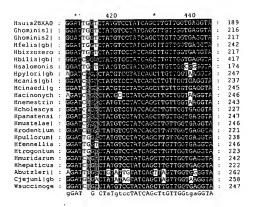


Figure 2 - 12

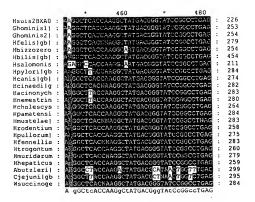


Figure 2 - 13

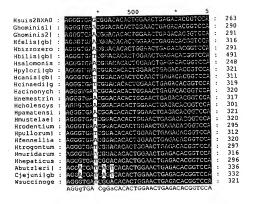


Figure 2 - 14

		20	*	540			
Hsuis2BXA0	:		CGGGAGGG	AGCAGTAGG	SAATATTECTCA	:	300
Ghominis11	:				GAATATTGCTCA	:	327
Ghominis2	:	GACTCCTA	JUGGSAGG0	:AGCAGTAGG	SAATATTSCTCA	:	328
Hfelis qb	:	GACTOCHA	rossnagge	AGCAGTAGG	SAATATTGCTCA	:	353
Hbizzozero	÷	SACTOON	CGGGAGGG	AGCAGTAGG	GAATATTGOTCA	:	328
Hbilis qb	:	GACTCCTA	COGGGGGG	RICAGTAUG	RATATTUCTCA	:	528
Hsalomonis	:	GACTUCEA	CGGGAGG:	CAGCAGTAGG	GAATATTGCTCA	:	285
Hpylori qb	:	GACTOCTA	CGGGAGG!	JAGCAGTAGG	gaa fatigotca	:	358
Hcanis gb	:	GACTICCTA	CGGGAGGG	CAGCAGTAGG	GAATATTGCTCA	:	348
Hcinaedilq	:	GACTCCT	CGGGAGG	CAGCAGTAGG	GAATATTGCTCA	:	356
Hacinonych	:	GACTCCT	REGGGAGG	CAGCAGTAGG	GAATATTGCTCA	:	357
Hnemestrin	:	GACTCCTA	CGGGAGG	CAGCAGTAGG	GAATATTGCTCA	:	354
Hcholescys	:	GACTCC'I/	ACGGGAGGG	CAGCAGTAGG	GAATATTGCTCA	:	338
Hpamatensi	:	GACTCCTA	CGGGAGG	CAGCAGTAGG	GAATATTGCTCA	:	358
Hmustelae	:	GACTCCT	CGGGAGG	CAGCAGTAGG	GAATATTGCTCA	:	357
Hrodentium	:				GAATATTGCTCA	:	332
Hpullorum	:	GACTCCTA	ACGGGAGGI	CAGCAGTAGG	GAATATTGCTCA	:	349
Hfennellia	:				GAATATTGCTCA	:	357
Htrogontum	:				GAATATTGCTCA	:	334
Hmuridarum	:				GAATATTGCTCA	:	353
Hhepaticus	:				GAATATTGC <u>T</u> CA	:	333
Abutzleri	:				GAATATTGCACA	:	373
Cjejunilgb	:				GAATATTGC <mark>G</mark> CA	:	369
Wsuccinoge	:				GAATATTGCTCA		358
		GACTCCT	ACGGGAGG	CAGCAGTaGG	GAATATTGCtCA		

Figure 2 - 15

Hsuis2BXA0 Ghominis1 Ghominis2		560 ATGGGGGAAA	COCHCOA				
Ghominis1				00260420660	GCGTGGAGG	:	337
		ATOOGGGAAS		GCAGCAACGCO		:	364
				SCAGCAACGCC		:	365
Hfelisighi	:			GCAGCAACGCC			390
Hbizzozero	:			GCAGCAACGCC			365
Hbilis qb	:			00004400406			565
Hsalomonis	:			GCAUCAACGCC			322
Hpylorilgb	:			UCAGCAAUGCC			395
Hcanis qb	:			GCAGCAACGCC			385
Hcinaedila	:			GCAGCAACGCC			393
Hacinonych	:			GCAGCAACGCC			394
Hnemestrin	:			GCAGCAACGCC			391
Hcholescys	:			GCAGCANCNCC			375
Hpamatensi	:			GCAGCAACGCC			395
Hmustelael	:			GCAGCAACGCC			394
Hrodentium	:			CAGCAACGCC			369
Hpullorum	:			GCAGCAACGCC			386
Hfennellia	:			GCAGCAACGCC			394
Htrogontum	:			GCAGCAACGCC			371
Hmuridarum	:			GCAGCAACGCC			390
Hhepaticus	:			GCAGCAACGCC			370
Abutzleril	:			GCAGCAACGCC			410
Cjejunijab	:			GCAGCAACGCC			406
Wsuccinoge	:			GCAGCAACGCC			395
msuccinoge	•			GCAGCAACGC			555

Figure 2 - 16

		600	*	620			
Hsuis2BXA0	:	ATGAAGGTTTTAGGAT	CCTA	AACTCCTTTT#T	AGAG	:	374
Ghominisl	:	ATGAAGGTTTTAGGAT	TGTA	aactocttttigt	AGAG	:	401
Ghominis21	:	ATGAAGGTTITAGGAT	TGTA	AACTCCTYTT:GT	AGAG	:	402
Hfelis gb	:	ATGRAGGTTTTAGGAT	TOTA	aactcotttiät	AGAC	:	427
Hbizzozero		ATGRAGGTTTTAGGAT	TOTA	AACTCCTTTT%T	AGAC	:	402
Hbilis qb	:	ATGAAGGTTTTAGGAT	TETA	AACTOCTTTT	AGAG	:	602
Hsalomonis	:	ATGAAGGTT7TAGGAT	TETA	AACTCCTTTIMI	AGAG	:	359
Hpylorijgb	:	ATGAAGGTTTTAGGAT				:	432
Hcanislabl	:	ATGAAGGTTTTAGGAT				:	422
Hoinaedilg	:	ATGAAGGTT!TAGGAT	TGTA	AACTCCXTTI	AAGAG	:	430
Hacinonych	:	ATGAAGGTTTTAGGAT	TGTA	AACTECTTTT	CAGAG	:	431
Hnemestrin	:	ATGAAGGTTTTAGGAT	TGTA	AACTCCTTTT	CAGAG	:	428
Hcholescys	:	ATGAAGGTTTTAGGAT	TGTA	AACTCCTTTTET	SAGAG	:	412
Hpamatensi	:	ATGAAGGTTTTAGGAT	ITGTA	AACTCCTTTTT	TAGAG	:	432
Hmustelae	:	ATGAAGGTTTTAGGAT	PTGTA	AACTCCTTTICT	AAGAG	:	431
Hrodentium	:	ATGAAGGTTTTCGGA"	TGTA	AACTCCTTTTCT	AGAC	:	406
Hpullorum!	:	ATGAAGGTTTTCGGA	TGT?	AACTOCTTTAT	TAGAC	:	423
Hfennellia	:	ATGAAGGTTTTAGGA'				:	431
Htrogontum	:	ATGAAGGTTTTAGGA				:	408
Hmuridarum	:	ATGAAGGTTTTAGGA'	FTGTA	AACTCCTTT!ÄT	GAGAG	:	427
Hhepaticus	:	ATGAAGGTTTTAGGA				:	407
Abutzleri!	:	ATGACACATTT CCCT				:	447
Cjejuni gb	:	ATGA CACTTTT CGCA				:	443
Wsuccinoge	:	ATGAAGGT TT GGA				:	432
		ATGAaggttTTaGGa	t tGT A	AACTCCTTTT T	agaG		

Figure 2 - 17

		*	640	*	660		
Hsuis2BXA0	:				TAAGCACCGGCT	:	410
Ghominis1	:	AAGA-T/	ATGACGGTA	TCTAA' GAA	TAAGCACCGGCT	:	437
Ghominis2	:	AAGA-TA	ATGACGGTA	TCT CAT SAA	TAAGCACCGGCT	:	438
Hfelis qb	:	AAGA-17	AFGACGGTA	TCT GAS GAA	TAAGCACCGGCT	:	463
Hbizzozero	:	AAGA-TA	ATGACGGTA	TCTGA: GF-	TAAGCACCGGCT	:	437
Hbilis qb	:	AAGA-TI	ATGACGGTA	TCTTA; GAA	TAAGCACCGGCT	:	638
Hsalomonis	:	AAGA-T/	ATGACGGTA	TCTCATGAA	PAAGCACCGGCT	:	395
Hpylorilgb	:	AAGA-TA	ATGACGGTA	TOTANGAA	TAAGCACCGGCT	:	468
Hcanis qb	:	AAGA-T	ATGACGGTA	TCTTA\GAA	TAAGCACCGGCT	:	458
Hcinaedilg	:	AAGA-T	ATGACGGIA	TCTTA GAA	TAAGCACCGGCT	:	466
Hacinonych	:				TAAGCACCGGCT		467
Hnemestrin	:	AAGE-T	ATGACGGTA	TCTAA GAA	TAAGCACCGGCT	:	464
Hcholescys	:				PAAGCACCGGCT	:	448
Hpamatensi	:				TAAGCACCGGCT	:	468
Hmustelae	:				TAAGCACCGGCK		467
Hrodentium	:				TAAGCACCGGCT		442
Hpullorum	:				TAAGCACCGGCT		459
Hfennellia	:				TAAGCACCGGCT		467
Htrogontum	:				TAAGCACCGGCT		444
Hmuridarum	:				TAAGCACCGGCT		463
Hhepaticus	:				TAAGCACCGGCT		443
Abutzleri	:		AATGACGGTA		TANGCACCGGCT		483
Cjejuni gb	:				TAAGCACCGGCT		480
Wsuccinoge	:				TAAGCACCGGCT		468
		AAGA T	aTGACGGTA	tct A GAa	TAAGCACCGGCT		

Figure 2 - 18

		* 680	*	700			
Hsuis2BXA0	:	AACTCCGTGCCAGCA	GCCGCGGTAAT	'ACGGAGGG'	CC :		447
Ghominis1!	:	AACTCCGTGCCAGCA					474
Ghominis2!	:	AACTCCGTGCCAGCA	GCCGCGGTAAT	'ACGGAGGG'	rga :		475
Hfelis qb	:	AMOTOGGTGCCAGCA	GCCGCGGTAAT	ACGGAGGG.	fCC :	:	500
Hbizzozero	:	AACTCCUTUCCAGCA	GCCGCGGTAAT	'ACGGAGGG'	: CC		474
Hbilis qb	:	AACTECGTGCCAGCA	GCCGCGGTAAT	'ACGGAGGG'	IGC :	:	675
Hsalomonis	:	AACTGGGTGGGAGCA	GCCGCGGTAAT	'ADGGAGGG	rgc :	:	432
Hpylori gb	:	AACTCCGTGCCAGCA	GCCGCGGTAAT	'ACGGAGGG	TGC :	:	505
Hcanis gb	:	AACTCCGTGCCAGCA	GCCGCGGTAAT	ACGGAGGG	TGC :	:	495
Hcinaedilg	:	AACTCCGTGCCAGCA	GCCGCGGTAAT	PACGGAGGG	: GC	:	503
Hacinonych	:	NACTCCGTGCCAGCA	GCCGCGGTAA1	PACGGAGGG	TGC :	:	504
Hnemestrin	:	AACTCCGTGCCAGCA	GCCGCGGTAAT	DDDAGDDAT	TGC :	:	501
Hcholescys	:	AACTCCGTGCCAGCA				:	485
Hpamatensi	:	NACTCCGTGCCAGCA	GCCGCGGTAM	PACGGAGGG	TGC	:	505
Hmustelael	:	NACTOOG1 GCCAGCA				:	504
Hrodentium	:	AACTCCGTGCCAGCA				:	479
Hpullorum	:	AACTCCGTGCCAGCA				:	496
Hfennellia	:	AACTCCGTGCCAGCA				:	504
Htrogontum	:	AACTCCGTGCCAGCA				:	481
Hmuridarum	:	NACTCCGTGCCAGCA				:	500
Hhepaticus	:	AACTGCGTGCC				:	464
Abutzleril	:	AACTCCGTGCCAGCA				:	520
Cjejunilgb	:	AACTCCGTGCCAGCA				:	517
Wsuccinoge	:	AACTCCGTGCCAGC#				:	505
		AACTCCGTGCCagca	gccgcggtaa	taCGGAGGG	TGC		

Figure 2 - 19

			720	*	740		
Hsuis2BXA0	:	AAGCGTTACT	CGGAATCACTGG	GCGTAAAGAG	TGCGT	:	484
Ghominis1	:	AAGCGTTACT	COGAATCACTGO	GCGTAAAGAG	NGCGT	:	511
Ghominis2	:	AAGCGTTACT	CSTAATCACTGG	GCGTAAAAA	TGCGT	:	512
Hfelis qb	:	MAGCGTTACT	CGCAATCMCTGC	GCGTAAAGAG	TGCGT	:	537
Hbizzozero	:	AAGCGTTACT	COGGAATCACTGG	GCGTAAAGAG	TGCGT	:	511
Hbilis qb	:	AAGCGTTACT	CGGAATCACTGG	GCGTARAGAS	GCCT	:	712
Hsalomonis	:	AAGCGTTACT	COGRATICACTO	CCHTAAAGAC	TGCGT	:	469
Hpylori gb	:	AAGCGTTACT	CGCAATCACTGC	GCGTAAAGAG	GCG?	:	542
Hcanis gb	:	AAGCGTTACT	CGGAATCACTGC	GCGTAAAGAG	GCGT	:	532
Hcinaedilg	:	AAGCGTTACT	CGGAATCACTGG	GCGTNAAGAC	TGCGT	:	540
Hacinonych	:	AAGCGTTAC7	COGRATCACTO	GCGTAAAGAG	GCGT	:	541
Hnemestrin	:		CGUAATCACTGO			:	538
Hcholescys	:	AAGCGTTACT	CGGAATCACTGC	CCCTAAAGA	GCGT	:	522
Hpamatensi	:		CGGAATCACTGC			:	542
Hmustelae	:	NACCGTTACT	TOGGAATCACTGO	GCGTNAAGAG	:::GCGT	:	541
Hrodentium	:		CCCAATCACTGO			:	516
Hpullorum	:		CEGAATCACTGO			:	533
Hfennellia	:		CGGAATCACTG			:	541
Htrogontum	:		CGGAATCACTGO			:	518
Hmuridarum	:		reggaateaete(:	537
Hhepaticus	:		rcggaatcactg(:	501
Abutzleri	:		rcggaatcactg			:	557
Cjejuni gb	:		CGGAATCACTG			:	554
Wsuccinoge	:		CCGGAATCACTG			:	542
		AAGCGTTAC	rcggaatcactg	GCGTAAAGa	3 gcGt		

Figure 2 -20

Hsuis2BXA0		* 760 * AGGCGGGAGACAGTCAGGBGTGAAATCCTATEGCT		52
Ghominis11	:	AGGCGGCAGGACAAGTCAGGTGTGAAATCCT T/GCT	:	541
Ghominis21	:	AGGGGGGGTT SAAGTCAGGTGTGAAATCCT T GCT	:	54
Hfelis qb	1	AGGGGGGGTT AS ARGTCAG TOT GAAATCCT TOTSCT	:	57
Hbizzozero	1	AGGUGGGTT AAAGTCAGGTGTGAAATCCTATEGCT	:	54
Hbilis qb	:	AGGCGGGAGERRAAGTCAGTTUTGAAATCCTGTAGCT		74
Hsalomonis	•			50
	:	aggoggg <mark>et</mark> ##aagtcag/tgtgaaatcctrt/Gct aggogggatr## <mark>C</mark> aglcag <mark>G</mark> tgtgaaatcct#t/Gct	:	57
Hpylori gb Hcanis gb	•	AGGCGGGAAGETAAGTCAGETGTGAAATCCTGTAGCT	•	56
Hcanis go	•		•	57
	:	AGGCGCGTAGTCAAGTCAC#TGTGAAATCCTGT <mark>A</mark> GCT AGGCGGGRT::::::MACTCAC#TGTGAAATCCT::TZGCT	:	57
Hacinonych Hnemestrin	1	AGGCGGGATANCCAGTCAGGTGTGAAATCCTATTGCT	•	57
Hcholescrin		AGGCGGGT A AAGTCAGATGTGAAATCCT TOGCT	•	55
Hoamatensi	•	AGGCGGGGT AND AAGTCAGNTGTGAAATCCTNT GCT	•	57
Hmustelae!	:	AGGCGGAGTSAWAAGTCAGHTSTGAAATCCTGTAGCT	:	57
Hrodentium	•	AGGCGGAT&CAAGTCAG TETGAAATCCT&TEGCT	•	55
Hpullorum	•	AGGCGGGTTGCAAGTCAGTTGTGAAATCCTATAGCT	:	51
Hfennellia	:	AGGCCGGATECCAAGTCAGGTGTGAAATGCTGTAGCT	:	5
Htrogontum	:	AGGCGGGGTÄAWAAGTCAGATGTGAAATCCTGTAGCT	ij	5
Hmuridarum		AGGCGGGGT#AFAAGTCAGFTGTGAAATCCT TAGCT	:	5
Hhepaticus	:	AGGCGGGGT: A AAGTCAG TGTGAAATCCT TAGCT		5
Abutzleril	:	AGGCGGATT AMGAGTTTS AGTGAAAT CCTATAGCT	:	5
Ciejunilab	:	AGGCGCATT TCAAGTCTCTTGTGAAATCTAATAGCT	:	5
Wsuccinoge	:	AGCCGCCTT CAAGTCAGATGTGAAATCCA CTGCT	:	5
wateringe	•	AGGCGGQ t aAGTcaq tGTGAAATcct t GCT		,
		Addedg to andread tolomatical t oci		

Figure 2 -21

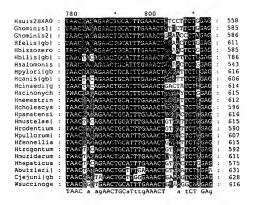


Figure 2 - 22

		820	*	840	*		
Hsuis2BXA0	:	TETGGGAGAGG	TAGGTGGAA	TTCTTGGTGT	AGGGGTA	: 5	95
Ghominis1	:	TSTGGGAGAGG	TARGTGGAA	TTCTTGGTGT	AGGGGTA	: 6	22
Ghominis2	:	TATGGGAGAGC	TAGGTGGAA	TTCTTGGTGT.	AGGGGTA	: 6	23
Hfelis gb	:	TFTGGGAGAGA	TAGGTGGAF	TTCTTGGTGT	AGGGGTA	: 6	48
Hbizzozero	:	TETGGGAGAGG	TAGGTGGAZ	TTCTTGGTGT.	AGGGGTA	: 6	22
Hbilis gb	:	TATGGGAGAGAG	TAUGIGGAA	TTCTTGGTGT	AGGGGTA	: 8	23
Hsalomonis	:	T@TGGGAGAGK	TAGGIGGAE	TTCTTGGTGT.	ACGGGTA	: 5	680
Hpylorilgb	:	TETCGCAGAGG	TAGGIGGA	STICTESGTGT.	AGGGGTA	: 6	553
Hcanis gb	:	TATOGGAGAG	TAGGIGGAA	TTCTTGGTGT	AGGGGTA	: 6	43
Hcinaedilg	:	TATGGGAGAG	TAGGTGGA	TTCTTGGTGT.	AGGGGTA	: 6	551
Hacinonych	:	TETGGGAGAG	YAGGTGGAA	TTCTTGGTGT	AGGGGTA	: 6	552
Hnemestrin	:	TATGGGAGAG	TAGGTGGA	TTCTTGGTGT	AGAGGTA	: 6	549
Hcholescys	:	TATGGGAGAG	TAGGTGGAA	TTCTTGGTGT	AGGGGTA	: 6	533
Hpamatensi	:	TATEGGAGAG				: 6	553
Hmustelae	:	TETGGGAGAGG	TAGGTGGA	TTCTTGGTGT	AGGGGTN	: 6	552
Hrodentium	:	TATGGGAGAG	STACGTGGAR	TTCTTGGTGT	AGGGGTA	: 6	527
Hpullorum	:	TATGGGAGAG	TAGGTGGA	TTCTTGGTGT	AGGGGTA	: 6	544
Hfennellia	:	TETGGGAGAG	TAGGTGGA	TTCTTGGTGT	AGGGGTA	: (552
Htrogontum	:	TSTGGGAGAGG	TAGGTGGA	TTCTTGGTGT	AGGGGTA	: (529
Hmuridarum	:	TETGGGAGAG	TAGGTGGA	TTCTTGGTGT	AGGGGTA	: (548
Hhepaticus	:			TTCTTGGTGT		: 1	512
Abutzleri	:	TOTGGGAGAG	TAGATGGA	TTTCTGGTGT.	AGGGGT?		668
Cjejunilgb	:	T@AGGGAGAG					665
Wsuccinoge	:			ATTCTCGGTGT		: 1	653
		T tGGGAGAGG	tAGgTGGAA	ATTCLLGGTGT	AGGGGTA		

Figure 2 - 23

		860		880		
Hsuis2BXA0	:	AAATCCGTAGAGATC	AAGAGGA	ATACTCATTGCGAAG	:	632
Ghominis1	:	AAATOOGTAGAGATO	AAGAGGA	ATACTCATIGCGAAG	:	659
Ghominis21	:	AAATCCGTAGAGATC	AAGAGGA	ATACTCATTGCGAAG	:	660
Hfelis gb	:	AAATCCGTAGAGATC	AAGAGGA	ATACTCATTGCGAAG	:	685
Hbizzozero	:	ANATOCOTAGRATO	AAGAGGA	ATACTCATTGCGAAG	:	659
Hbilis gb	:	ABATCCCTAGAGATC	AAGAGGA	ATACTCATTGCGAAG	:	860
Hsalomonis	:	AAATCCGTAGAGAT	AAGAGGA	ATACTCATTGCGAAG	:	617
Hpylorilgb	:	AAATCCGTAGAGATC	CAAGAGGA	ATAUTCATTGCGAAG	:	690
Hcanis gb	:	AAATCCGTAGAGATC	CAAGAGGA	ATACTCATTGCGAAG	:	680
Hcinaedilg	:	AAATCCGTAGAGATC	AAGAGGA	ATACTCATTGCGAAG	:	688
Hacinonych	:	AAATCCGTAGAGATC	AAGAGGA	ATACTCATTGCGAAG	:	689
Hnemestrin	:			ATACTCATTGCGAAG	:	686
Hcholescys	:	AAATCCCCAGAGATC	CAAGAGGA	ATACTCATTGCGAAG	:	670
Hpamatensi	:	AAATCCUTAGAGATC	CAAGAGGA	ATACTCATTGCGAAC	:	690
Hmustelae	:	AAATCCGTAGAGATC	CAAGAGGA	ATACTCATTGCCAAG	:	689
Hrodentium	:	AAATCCCTAGAGATC	IAAGAGG2	ATACTCATTGCGAAC	:	664
Hpullorum	:			ATACTCATTGCGAAG	:	681
Hfennellia	:			ATACTCATTGCGAAC	:	689
Htrogontum	:			ATACTCATTGCGAAG	:	666
Hmuridarum	:			ATACTCATTGCGAAC	:	685
Hhepaticus	:			ATACTCATTCCGAAC		649
Abutzleri	:			ATAC <mark>CG</mark> ATTGCGAAG		705
Cjejuni gb	:			ATACCCATTGCGAAG		702
Wsuccinoge	:			ATACTCATTGCGAAG		690
		AAATCCGtAGAgATC	CaagAgGA	ATACtcATTGCGAAG		

Figure 2 - 24

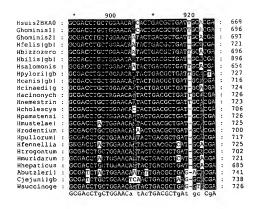


Figure 2 - 25

		*	940		960		
Hsuis2BXA0	:	AAGCGTGG	GGAGCAAACAG	GATTAGATAC	CCTGGTAG	:	706
Ghominis1	:	AAGCGTGG	GAGNAAACAG	GATTAGATAC	CCTGGTAG	:	733
Ghominis2	:	AAGCGTGG	GGAGCAAACAG	GATTAGATAC	CCTGGTAG	:	734
Hfelis gb	:	AAGCGTGGG	BUAGCAAACAG	GATTAGATAC	CCTGGTAG	:	758
Hbizzozero	:	AAGCGTGG	SSAGCAAACAG	GATTAGATAC	CCTGGTAG	:	733
Hbilis gb	:	AAGCGTGG	GGAGCAAACAS	GATTAGATAC	CCTGGTAG	:	933
Hsalomonis	:	AAGCGTCS	GGAGCAAACAG	GATTAGATAC	CCTGGTAC	:	691
Hpylorilgb	:	AAGCGTGG	JOAGCAAACAG	GATTAGATAC	CCTCGTAG	:	764
Hcanis gb	:	AAGC-TGG	GGAGCAAACAG	GATTAGATAC	CCTGGTAG	:	752
Hcinaedilq	:	AAGCGTGG:	GCAGCAAACAG	GATTAGATAC	CCTGGTAG	:	761
Hacinonych	:	AAGCGTGG	GGAGCAAACAG	GATTAGATAC	CCTGGTAG	:	763
Hnemestrin	:	AAGCGTGG	GGAGCAAACAG	GATTAGATAC	CCTGGTAG	:	760
Hcholescys	:	AAGCGTGG	GGAGCAAACAG	GATTAGATAG	CCTGGTAC	:	743
Hpamatensi	:	AAGGGTGG	UGAGCAAACAG	GATTAGATAC	CCTGGTAG	:	763
Hmustelae	:	AAGCGTGG:	GGAGCAAACAG	GATTAGATAG	CCTGGTAG	:	762
Hrodentium	:	AAGCGTGG	GGAGCAAACAG	GATTAGATA:	CCTGGTAG	:	73
Hpullorum!	:	AAGC-TGC	GGAGGAAAGAG	GATTAGATAG	CCCTGGTAG	:	753
Hfennellia	:		OGAGRAAACAG			:	762
Htrogontum	:	AAGCGTGG	GGAGCAAACAG	GATTAGATAG	CCTGGTAG	:	739
Hmuridarum	:	AAGCGTGG	GGAGCAAACAG	GATTAGATAG	CCTCGTAG	:	751
Hhepaticus	:		GGAGCAAACAG			:	723
Abutzleri	:		GGAGCAAACAG			:	771
Cjejunilgb	:		GGAGCAAACAG			:	77
Wsuccinoge	:		GGAGCAAACAG			:	763
		AAGCgTGG	GGAGCAAACAG	GATTAGATA	CCCTGGTAG		

Figure 2 - 26

		*	980	*	100		
Hsuis2BXA0	:	TCCACGCCCTA	AACGATGGAT	GCTAGTTGTTC	GGAG	:	743
Ghominisl	:	TOCACGCCCTA	AACGATO <mark>G</mark> AT	SCTAGTTGTTC	G-AGE	:	769
Ghominis2	:	TOCACGCCCTA	AACGATCGAT	GCTAGTTG FTC	GGGGC	:	771
Hfelis gb	:	TOCADGCCCTA	AACGATGGAT	SCIAGITGITO	GGGGC	:	795
Hbizzozero	:	TOCACGCCCTA	AACGATOGAT	SCTAGTIGTTO	GGGGG	:	770
Hbilis gb	:	TCCACGCCCT/	AACGATCAAT	GCTAGTTGTTO	CCCTC	:	970
Hsalomonis	:	TOCACGCCCTA	AACGATC <mark>G</mark> AT	GCTACTTGTTC	GGGGG	:	728
Hpylorilgb	:	TCCACGCCCT;	LACCATO <mark>C</mark> AT	SCTACTTGTTC	GAGGE	:	801
Hcanis gb	:	TCCACGCCCTA	AACGATGAAT	GCTAGTTGTTC	CCCTC	:	789
Hcinaedi g	:	TCCACGCCCTA	AACGATEAAT	GCTNGTTGTTC	CCCTC	٠.	798
Hacinonych	:	TCCACGCCCT	AACGATGGAT	GCTAGTTGTT(GRGGC	:	800
Hnemestrin	:	TCCACGCCCTA				:	797
Hcholescys	:	TCCACGCCCTZ	AACGAT SAAT	GCTAGTTGTT	GGGTG	:	780
Hpamatensi	:	TCCACGCCCT/				:	800
Hmustelae	:	TCCACGCCCTA				:	799
Hrodentium	:	TOCACGCCCTA				:	774
Hpullorum	:	TCCACGCCCT?				:	790
Hfennellia	:	TCCACGCCCTA				:	799
Htrogontum	:	TCCACGCCCT/				:	776
Hmuridarum	;	TCCACGCCCTA				:	795
Hhepaticus	:	TCCACGCCCTA				:	759
Abutzleri	:	TCCACGCCCTA				:	815
Cjejuni gb	:	TCCACGCCCT				:	812
Wsuccinoge	:	TCCACGCCCT				:	800
		TCCACGCCCTA	AAACGATG At	gCTAGTTGTT	G G		

Figure 2 - 27

		0	*	1020	*		
Hsuis2BXA0	:	CTTTGTC	TTTC	CAGTAATGCAGCTAAC	GCCTTAAGCA	:	780
Ghominis1	:	CTTTGTC	TTTC	CAGTAATGCA <mark>CG</mark> TAAC	GCCTTAARNA	:	806
Ghominis2	:	CTTTGTC	CTCC	CAGTAATGCAGCTAAC	GCCTTAAGCA	:	808
Hfelis qb	:	CTT-CT	CTCC	CACTARTGCAGCTARC	GOGTTAAGCA	:	831
Hbizzozero	:	CTTTGTC	CCCC	CAGTAATGCAGCTAAC	GCCTTAAGCA	:	807
Hbilis qb	:	CTT-GTG	AGGG	CAGTAATGTAGCTAAC	GORTTAAGCA	:	1006
Hsalomonis	:	CTTTGTC	cccc	CAGTAATGCAGCIAAC	GCCTTAAGCA	:	765
Hpylori gb	:	CTTAGTO	TCTC	CAUTAAT GCAGC PAAC	GCETTAAGCA	:	838
Hcanis gb	:	CTT-GT	AGGG	CAGTAATGCAGCTAAC	GCMTTAAGCA	:	825
Hcinaedilg	:	CTT-NTO	AGGG	CAGTAATGCAGCTAAC	gcMttaagca	:	834
Hacinonych	:	CTTTCTC	YYYC	CAGTAATGCAGCTAAC	GCCTTAAGCA	:	837
Hnemestrin	:	CTTAGTO	TCTC	CAGTAATGCA <mark>CG</mark> TAAC	GCMTTAAGCA	:	834
Hcholescys	:	CINE - CIN	ACTO	CAGTAATGCAGCTAAC	GCATTAAGCA	:	816
Hpamatensi	:			CAGTAATGCAGCTAAC		:	836
Hmustelae	:	CTT - CTC	ACTO	CAGTAATGCAGTTAAC	ACHTTAAGCA	:	835
Hrodentium	:			CAGTAATGCAGCTAAC		:	810
Hpullorum!	:			CAGTAATGCAGCTAAC		:	826
Hfennellia	:			CAGTAATGCAGCTAAC		:	835
Htrogontum	:			CAGTANTICAGE FAAC		:	812
Hmuridarum	:			CAGTAATGCAGCTAAC			831
Hhepaticus	:			CAGTAATGCAGCTAAC		:	795
Abutzlerii	:			CAGTAATGCAGTTAAC			851
Cjejuni gb	:			CAGTAATGCAGCTAAC			848
Wsuccinoge	:			CAGTAATGCAGTTAAC		:	836
		CTt Gto	3	CAGTAATGCAgcTAAC	gC TTAAGca		

Figure 2 - 28

		1040		1060	*		
Hsuis2BXA0	:	ncececen	GGGGAGTAC	GGTCGCAAGAT	TTAAAACTCA	:	817
Ghominisl	:	Tec-geer	GGGGAGTAC	GTCCCAAGA:	TAAAACTCA	:	842
Ghominis21				ggT0gCAAGA1		:	845
Hfelis gb				GGTCGCAAGAT		:	868
Hbizzozero	:			GGTCGCAAGAT		;	844
Hbilis qb	:	TREEGGET	GGGGAGTAC	ggTCGCAAGA1	TAAAACTCA	:	1043
Hsalomonis	:	resegger	GOGGAGTAG	GGTCGCAAGA"	FTAAAACTCA	:	802
Hpylori qb	:	TOUCGOOD	GGGGAGTAC	GGTCGCAAGA1	TAAAACTCA	:	875
Heanis [qb]	:	TECCSCCT	GGGGAGTAC	GGTCGCAAGA"	TTAAAACTCA	:	862
Hcinaedilq	:	TECCCCT	GGGGAGTAC	GGTCGCAAGA1	TTAAAACTCA	:	871
Hacinonych	:	TCRCGGGT	GGGGAGTAC	GSTCGCAAGA'	TTAAAACTCA	:	874
Hnemestrin	:	TCCCGCCT	GGCGAGTAC	GGTCGCAAGA'	TTAAAACTCA	:	871
Hcholescys	:	TROCGCCT	GGGGAGTAC	GGTCGCAAGA"	TTAAAACTCA	:	853
Hpamatensi	:	TECCCCC	GGGGAGTAC	GGTCGCAAGA'	TTAAAACTCA	:	873
Hmustelael	:	TECCGCCT	GGGGAGTAC	GGTCGCAAGA'	FFAAAACTCA	:	B72
Hrodentium	:	TECCCCC	GGGGAGTAC	GGTCGCAAGA	PTAAAAACTCA	:	847
Hpullorum	:	TICCGCCT	UGUGAGTAC	GGTCGCAAGA	TTAAAACTCA	:	863
Hfennellia	:	TECCCCCT	GEGGAGTAC	GGTCGCAAGA'	TTAAAACTCA	:	872
Htrogontum	:	TTCCGCC"	GGGGAGTAC	GG PCGCAAGA	TTAAAACTCA	:	849
Hmuridarum	:	TTCCGCCT	GGGGAGTAC	GGTCGCAAGA	TTAAAACTCA	:	868
Hhepaticus	:	TECCGCCT	GGGGAGTAC	GGTCGCAAGA	TTAAAACICA	:	832
Abutzleri	:	TACCGCCT	GGGGAGTAC	GGTCGCAAGA	TTAAAACTCA	:	888
Cjejunilgb	:	TACCGCCT	GGGGAGTAC	GGTCGCAAGA	TTAAAACTCA	:	885
Wsuccinoge	:	TECCCCCT	GGGGAGTAC	GGTCGCAAGA	TTAAAACTCA	:	873
		T CcGCCT	GGGGAGTAC	GGTCGCAAGA	TTAAAACTCA		

Figure 2 - 29

		1080	*	1100			
Hsuis2BXA0	:	AAGGAATAGAC	GGGACCCG	CACAAGCGGTG	GAGCAT	:	854
Ghominisl	:	AAGGAATAGAC	GGGGACC-GG	CACAAGCGGTG	GAGCAT	:	878
Ghominis2	:	AAGGAATAGAC	aggaacc c ac	CACAAGCGGTG	GAGCAT	;	882
Hfelis gb	:	AAJGAATAGAC	EGGGACCCG	CACAAGCHINN	NEMERS	;	905
Hbizzozero	:	AAGGAATAGAC	agggauc c g	CACAAGCGGTG	GAGCAT	:	881
Hbilis gb	:	AAGGAATAGAC	9666465666	DACAAGOGGTG	GAGCAT	:	1080
Hsalomonis	:	AAGGAATAGAC	GGGACOCG	CACAAGCGGTG	GAGCAT	:	839
Hpylori gb	:	AAGGAATAGAC	GGGGACCCG	CACAAGCGGTG	GAGCAN	:	912
Hcanis[gb]	:	AAGGAATAGAC	GGGGACCCG(CACAAGCGGTG	GAGCAT	:	899
Hcinaedilg	:	AAGGAATAGAC	GGGGACCCG	CACAAGCGGTG	GAGCAT	:	908
Hacinonych	:	AAGGAATAGAC	GGGGACCCG	CACAAGCGGTG	GAGNNN	:	911
Hnemestrin	:	AAGGAATAGAC	GGGGACCCG:	CACAAGCGGTG	GAGCAT	:	908
Hcholescys	:	AAGGAATAGAC	GGGGACCCG	CACAAGCGGTG	GAGCAT	:	890
Hpamatensi	:	AAGGAATAGAC	GGGGACCCG	CACAAGOGGTG	GAGCNM	:	910
Hmustelae	:	AAGGAATAGAC	GGGGACCCG	CACAAGCGGTG	GAGCAT	:	909
Hrodentium	:	AAGGAATAGAC	GGGGACCCG	CACAAGCGGTG	GAGCAT	:	884
Hpullorum	:	AAGGAATAGAC	GGGGACCCG	CACAAGCGGTG	GAGCAT	:	900
Hfennellia	:	AAGGAATAGAC	GGGGACCCG	CACAAGCGGTG	GAGCAT	:	909
Htrogontum	:	AAGGAATAGAC	GGGGACCCG	CACAAGCGGTC	GAGCAT	:	886
Hmuridarum	:	AAGGAATAGAC	GOGGACCCG	CACAAGCGGTG	GAGNNN	:	905
Hhepaticus	:	AAGGAATAGAC				:	869
Abutzleri	:	AAGGAATAGAC				:	925
Cjejunilgb	:	AAGGAATAGAC				:	922
Wsuccinoge	:	AAGGAATAGAC				:	910
		AAGGAATAGAC	GGGGACCcG	CACAAGCGGTC	GAGCAT		

		1120 * 1140			
Hsuis2BXA0	:	GTGGTTTAATTCGAAGTTACACGAAGAACCTTA	CCTA	:	891
Ghominisl	:	GTGGTTTAATTCGAAGATAC <mark>A</mark> CGAAGAACCTTA	CCTA	:	915
Ghominis2	:	GTGGTTTAATTCGAAGATAC <mark>A</mark> CGAAGAACCTTA	CCTA	:	919
Hfelis qb	:	GTGGTTTAATTCGANNNWWW.CGAAGAACCTTA	CCTA	:	942
Hbizzozero	:	GTGGTTTAATTCGAAGATACACGAAGAACCITA	CCTA	:	918
Hbilis gb	:	GTGGTTTAATTCGAAGATACXCGAAGAACCTTA	CCTA	:	1117
Hsalomonis	:	GTGGTTTAATTCG/TGCTACACGAAGAACCTTA	CCTA	:	876
Hpylorijab	:	GTGGTTTAATTCGANNNHACACGAAGAACCTTA	CCTA	:	949
Hcanis gb	:	GTGGTTTAANTCGAAGATAC#SGAAGAACCTTA	CCTA	:	936
Hcinaedijq	:	GTGGTTTAATTCGAGTATAC CGAAGAACCTTA	CCTA	:	945
Hacinonych	:	GTGGTTTAATTCGANNNNNCACGAAGAACCTTA	CCTA	:	948
Hnemestrin	:	GTGGTTTAATTCGAAGGTAC KUGAAGAACCTTA	CCTA	:	945
Hcholescys	:	gtggtttaattcgaagatac;;cgaagaacctta	CCTA	:	927
Hpamatensi	:	GTGGTTTAA1TCGAMNNTACECGAAGAACCTTA	CCTA	:	947
Hmustelae	:	gtggtttaattcgaknntac@cgaagaacctta	CCTA	:	946
Hrodentium	:	GTGGTTTAATTCGAAGATACACGAAGAACCTTA	CCTA	:	921
Hpullorum	:	GTGGTTTAATTCGAAGATAC CGAAGAACCTTA	CCTA	:	937
Hfennellia	:	GTGGTTTAATTCGAANNTAC#CGAAGAACCTTA	CCTA	:	946
Htrogontum	:	GTGGTTTAATTCGAAGATAC%CGAAGAACCTTA	CCTA	:	923
Hmuridarum	:	GTGGTTTAATTCGANNNNAC CGAAGAACCTTA	CCTA	:	942
Hhepaticus	:	GTGGTTTAATTCGAAGATAC∰CGAAGAACCTTA		;	906
Abutzleri	:	GTGGTTTAATTCGANNNACACGAAGAACCTTA		:	962
Cjejunilgb	:	GTGGTTTAATTCGAAGNTAC@CGAAGAACCTTA		:	959
Wsuccinoge	:	GTGGTTTAATTCGANNNACHCGAAGAACCTTA		:	947
		GTGGTTTAATTCGAagaTAC CGAAGAACCTTA	CCTa		

Figure 2 -31

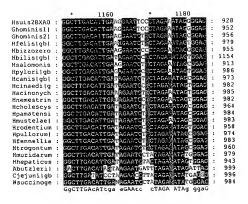


Figure 2 - 32

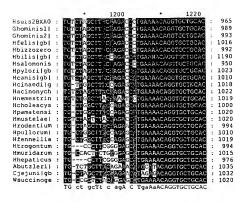


Figure 2 - 33

		*	1240		12	
Hsuis2BXA0	:	GGCTGTCGTC	AGCTCGTGTCG	TGAGATGTT	GGTTAA :	1002
Ghominis1	;	GGCTGTCGTC	AGCTCGTGTCG	TGAGATGTT	GGTTAA :	1026
Ghominis2	:	GGCEGTCGTC	AGCTOGTGTCG	TGAGATGTT	GGGTTAA :	1030
Hfelis gb	:	GGCTGTCGTC	ASCTOSTSTOS	reagater:	GGGTTAA :	1053
Hbizzozero	:	GGCTGTCGTC	AGCTCGTGTCG	TGAGATGTT	GGTTAR :	1029
Hbilis qb	:	GCCTGTCGTC	AGCTOSTGTOS	TGAGATGTT	GGTTAF :	1227
Hsalomonis	:	ecorerecte	AGCTCGIGTCG	TGAGATGTT	GGTTAA :	987
Hpylorilgb	:	GGCTGTCGTC	AGCTCGTGTCG	TGAGATGTT	GGGTTAF :	1060
Hcanis gb	:	SECTETOSTO	AGCTCGTGTCG	TGAGATGTT	GGTTAA :	1047
Hcinaedilg	:	GGCTGTCGTC	AGCTCGTGTCG	TGAGATCTT	GGTTAA:	1055
Hacinonych	:	GECTETCETC	AGCTCGTGTCG	TGAGATGTT	GGGTTNA :	1059
Hnemestrin	:	GGCTGTCGTC	AGCTCGTGTCG	TGACATGIT	GGGTTAA :	1056
Hcholescys	:	GGCTGTCGTC	ACCTCGTGTCG	TGAGATGTT	GGGTTAA:	1037
Hpamatensi	:	GGCTGTCGTC	AGCTCGTGTCG	TGAGATGTT	GGGTTAA :	1057
Hmustelae	:	GGCTGTCGTC	AGCTCGTGTCG	TGAGATGTT	GGGTTAA :	1057
Hrodentium	:	GGCTGTCGTC	ACCTOCTOTO	TGAGATGTT	GGTTAP :	1031
Hpullorum!	:	GGCTGTCGTC	AGCTCGTGTCG	TGAGATGTT	GGGTTAA :	1047
Hfennellia	:	GGCTGTCGTC	AGCTCGTGTCG	TGAGATGIT	GGTTAA:	1056
Htrogontum	:	GGCTGTCGTC	AGCTCGTCTCG	TGAGATGTT	GGGTTAA :	
Hmuridarum	:	GGCTGTCGTC	AGCTCGTGTCG	TGAGATGTT	GGTTNA :	
Hhepaticus	:	GGCTGTCGTC	AGCTCGTGTCG	TGAGATGTT	GGGTTAA :	1013
Abutzleri	:	GGCTGTCGTC	AGCTCGTGTCG	TGAGATGTT	GGGTTAA :	
Cjejuni gb	:	GGCTGTCGTC	AGCTCGTGTCG	TGAGATGTT	GGGTTNA :	
Wsuccinoge	:		AGCTCGTGTCG			1057
		GGCTGTCGTC	AGCTCGTGTCG	TGAGATGTT	GGGTTAA	

Figure 2 - 34

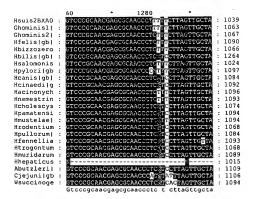


Figure 2 - 35

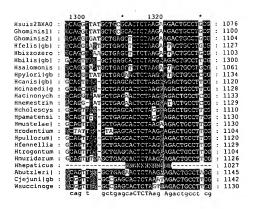


Figure 2 - 36

		1340		1360		
Hsuis2BXA0	:	TAAGCAGGAGGA	AGGTGAGGAC	GACGTCAAGTCATC	12 :	1113
Ghominisl!	:	TAANAGGA	AGGTGAGGAC	GACGTCAAGTCATC	担:	1133
Ghominis2	:	TAAGCANGAGGA	AGGTGAGGAC	GACGTCAAGTCATC	12 :	1141
Hfelis gb	:	TAAPCAGGAGGA	AGGTGAGGAC	GACGTCAAGTCATC	14 :	1164
Hbizzozero	:	TAAGCAGGAGGA	AGGTGAGGAC	GACGTCAAGTCATC	Z :	1140
Hbilis gb	:	TAAGGAGGA	AGGTGAGGAC	GACGTCAAGTCATC	14 :	1337
Hsalomonis	:			GACGYTAAGTCATC		1098
Hpylorilgb	:			GACGTCAAGTCATC		1171
Hcanis gb	:			GACGTCAAGTCAT		1157
Hcinaedilg	:			GACGTCAAGTCAT		1165
Hacinonych	:			GACGTCAAGTCAT(1170
Hnemestrin	:			GACGTCAAGTCAT		1166
Hcholescys	:			GACGTCAAGTCAT		1147
Hpamatensi	:			GACGTCAAGTCAT		1167
Hmustelae!	:			GACGTTAAGTCAT		1167
Hrodentium	:			GACGTCAAGTCAT		1141
Hpullorum	:			GACGTCAAGTCAT:		1157
Hfennellia	:			GACGTCAAGTCAT		1166
Htrogontum	:			GACCTCAAGTCAT		1141
Hmuridarum	:			GACGTCAAGTCAT	<u> </u>	1163
Hhepaticus	:	NEWNINNE			:	1053
Abutzleri	:			GACGTCAAGTCAT		1182
Cjejunilgb	:			GACGTCAAGTCAT		1179
Wsuccinoge	:			GACGTCAAGTCAT		1167
		taaG aggAGGA	AAGGTGaGGAc	:GACGTcAagtcat	ca	

Figure 2 - 37

		* 1	380	*		1400			
Hsuis2BXA0	:	TESCCCTT	ACGCCTA	GGGCTA	CACACO	TGCTA	CAATG	:	1150
Ghominis1	:	TEGCCCTT	ACCCCTA	GGGCTA	CACACO	TGCTA	CAATG	:	1170
Ghominis2	:	TEGECEST	ACHCCTA	GGGCTA	CACACO	TGCTA	CAATO	:	1178
Hfelis qb	:	TGGCCCTT	ACCCCTA	GGGCTA	CACACO	TGCTA	CAATC	:	1201
Hbizzozero	:	TGGCCCTT	ACCCCTA	GGGCTA	CACACO	TGCTA	CAATO	:	1177
Hbilis qb	:	TEGCCCTT	CGCCTA	GGGCTA	CACACO	TGCTA	CAATG	:	1374
Hsalomonis	:	TESCCCT1	ACCOUNT	GGGCTA	CACAC	STECTA	CAATG	:	1135
Hpylorilgb	:	TEGECCETT	MOGCOTA	GGGCTA	CACACO	STGCTA	CAATC	:	1208
Hcanis gb	:	TEGECCETT	ACGCCTA	GGGCTA	CACACO	STGCTA	CAATG	:	1194
Hcinaedilg	:	TGGCCCTT	PACGCCTA	GGGCTA	CACAC	STGCTA	CAATO	:	1202
Hacinonych	:	TEGCCCTI	PACGCCTA	GGGCTA	CACACO	STGCTA	CAATG	:	1207
Hnemestrin	:	TEGCCCTT	PACGCCTA	GOGCTE	CACAC	STGCTA	CAATC	:	1203
Hcholescys	:	TEGCCCTI	PACCECTA	GGGCTA	CACAC	STGCTA	CAATG	:	1184
Hpamatensi	:	TGGCCCTT	PACGCCTA	GGGCTA	CACAC	STGCTA	CAATG	:	1204
Hmustelae	:	TGGCCCTT	PACGCCTA	GGGCTA	CACAC	STGCTA	CAATG	:	1204
Hrodentium	:	TEGOCCET	PACGCCTA	GGGCT	CACAC	STECTA	CAATG	:	1178
Hpullorum	:	TGGCCCT1	PACGCCTF	GGGCTA	CACAC	STGCTA	CAATG	:	1194
Hfennellia	:	TGGCCCTT	PACGCCTA	GGGCT#	CACAC	STGCTA	CAATG	:	1203
Htrogontum	:	TGGCCCTT						:	1178
Hmuridarum	:	TGGCCCT	PACGCCTA	GGGCT	CACAC	GTGCTA		:	1200
Hhepaticus	:		N					:	1057
Abutzleri	:	TGGCCCT:						:	1219
Cjejunilgb	:	TGGCCCT						:	1216
Wsuccinoge	:	TGGCCCT						:	1204
		tggcccti	Acgccta	gggcta	cacac	gtgcta	caATG		

Figure 2 - 38

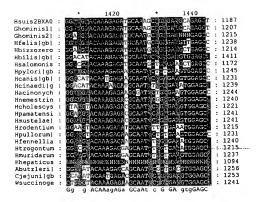


Figure 2 - 39

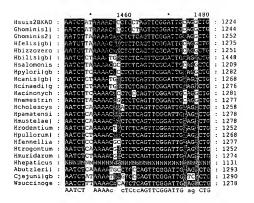


Figure 2 -40

	Eb.	1 035 219 A1			
		1500	÷ 1		
			1		1261
Hsuis2BXA0	CAACTOG <mark>CCTG</mark> CAT			:	
Ghominisl	:AACTCO <mark>C</mark> CT <mark>G</mark> CAT			:	1281
Ghominis2	caact co <mark>c</mark> ct <mark>s</mark> cat			:	1289
Hfelis gb	CACOTOC COTOCAT			:	1312
Hbizzozero	PAACTOGOCT GCAT			:	1288
Hbilis qb	гар@то@отраас	A4AGCTGGAA1	POGCTAGTARTOG	:	1485
Hsalomonis	CACOTOCOTOCAC	GAAGCTGGAAT	POGCTAGTAATOG	:	1246
Hpylorilgb	CAACTOU <mark>CCT</mark> GCAI	GAAGCTGGAAT	POGCTAGTAATOG	:	1319
Hcanis qb	DAACTOG GOTTICAT	GAAGCTGGAAT	CCCTAGTAATCC	:	1305
Hcinaedilg	CAACTOCKCT4CA1	AAGCTGGAAT	CGCTAGTAATCG	:	1313
Hacinonych	CAACTCGCCTGCAT	GAAGCCGGAA"	CGCTAGTAATCG	:	1318
Hnemestrin	CAACTCGCCTGCAT	GAAGCTGGAAT	CCCTAGTAATCC	:	1314
Hcholescys	CAACTCGGCTGCA	GAAGCTGGAAT	CCCTACTAATCC	:	1295
Hpamatensi	CAACTCGGCTGCA:			:	1315
Hmustelae	CAACTCGGCTACA	rgaagctggaat	TCGCTAGTAATCG	:	1315
Hrodentium	CAACTOOCTOCA	FGAAGCTGGAAT	TOGOTAGTAATOG	:	1289
Hpullorum	CAACTUGACTACA	FGAAGCTGGAAT	CGCTAGTAATCG	:	1305
Hfennellia	CAACTOG CTICA	AAGCTGGAA1	ICGCTAGTAATCG	:	1314
Htrogontum	CAACTOGMOTMCA	AAAGCTGGAAT	PCGCTAGTAATCG	:	1289
Hmuridarum	CAACTCGGCTMAA	FGAAGCTGGAA1	PCGCTAGTAATCG	:	1311
Hhepaticus	งทยเลยเกรียนสู้จน:	INNINHHHMMM	HAMMANAMAN H	:	1168
Abutzleri	CAACTOCKCTACA	GAACTTGGAA	regetagtaateg	:	1330
Cjejunilgb	CAACTCG GAGCA	rgaago <mark>o</mark> ggaat	regetagtaated	:	1327
Wsuccinoge	CAACTCGACTACA	TGAAGCT'GGAA'	TCGCTAGTAATCC	:	1315
	CAACTCG ct CA	TgAAGc tGGAA	TCGCTAGTAATCG		

Figure 2 - 41

		520		1540	*		
Hsuis2BXA0	:	AATCAGUI	ATGT	CGGTGAATA	CGTTCCCGGGTC	:	1298
Ghominisl	:	AATCAGOT	ATGT	CGGTGAATA	CGTTCCCGGGTC	:	1318
Ghominis2	:	MAATCAGC	ATGTS	COGTGAATA	CGTTCCCGGGGTC	:	1326
Hfelis gb	:	AATCAGC:	AIGT: 0	CGGTGAATA	CGITCCCGGGGTC	:	1349
Hbizzozero	:	MAATCAGC	ATGTS	CGGTGAATA	CGTTCCCGGGTC	:	1325
Hbilis gb	:	TGAATCAGO	ATGTC	CGGTGAATA	CGTTCCCGGGTC	:	1522
Hsalomonis	:	BAATCAGC:	ATGT	CGGTGAATA	CGTTCCCGGGCTC	:	1283
Hpylori gb	:				CGTTCCCGGGGTC	:	1356
Hcanisigbi	:				CGTTCCCGGGTC	:	1342
Hcinaedilg	:	AATCAGC	ATCT#	CGGTGAATA	CGTTCCCGGGTC	:	1350
Hacinonych	:				CGTTCCCGGGTC		1355
Hnemestrin	:				CHTTCCCGGGTC		1351
Hcholescys	:				CGTTCCCGGGTC		1332
Hpamatensi	:				CGTTCCCGGGTC		1352
Hmustelae	:				CGTTCCCGGGTC		1352
Hrodentium	:				CGTTCCCGGGTC		1326
Hpullorum	:				CGTTCCCAGGTC		1342
Hfennellia	:				CGTTCCCGGGTC		1351
Htrogontum	:				CGTTCCCGGGTC		1326
Hmuridarum	:				CGTTCCCGGGTC		1348
Hhepaticus	:				CGTTCCCGGGTX	1:	1205
Abutzleril	:				CGTTCCCGGGTC		1367
Cjejunilgb	:				CGTTCCCGGGTC		1364
Wsuccinoge	:				CGTTCCCGGGTC		1352
		aATCAGC	MIGE	CGGTGAATA	CGTTCCCGGGTC		

Figure 2 - 42

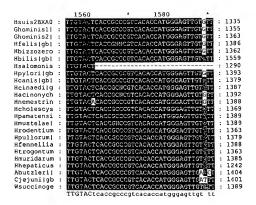


Figure 2 - 43

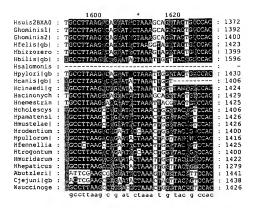


Figure 2 - 44

		*	1640	*	1660		
Hsuis28XA0	:	CCCAC	ACACAGCGAC	CECETGAAGT	CGTAACAAGGT	:	1409
Ghominis1	:		ACACAGCGAC'			:	1414
Ghominis2	:					:	1422
Hfelis qb	:	GGCAC	ACACAGCGAC'	eeeee		:	1443
Hbizzozero	:		ACACAGCGAC			:	1421
Hbilis qb	:	GGC 46	ATGCAGCGAC	regee		:	1616
Hsalomonis	:					:	-
Hpylori qb	:	ECC AC	ACACAGCGAC"	(GGGG		:	1450
Hcanis gb	:					:	_
Hcinaedilg	:	GGC #G	ATGCAGCGAC	reced		:	1444
Hacinonych	:	GGCAC	ACACAGCGAC	rgggg		:	1449
Hnemestrin	:	CGCAC	ACACAGCGAC'	TGGGGTGAAGT	CGTAACAAGGT	:	1462
Hcholescys	:		ATGCAGCGAC'			:	1425
Hpamatensi	:		ATGCAGCGAC'			:	1446
Hmustelae	:	GGC.38	TNS			:	1435
Hrodentium	:	GGC To	ATGCAGCGAC	recectica		:	1423
Hpullorum	:		ATGCAGC			:	1428
Hfennellia	:					:	1445
Htrogontum	:	GGC	ATGCAGCGAC'	TGGGGTG		:	1422
Hmuridarum	:						1442
Hhepaticus	:				- 		1302
Abutzleril	:						1461
Cjejuni gb	:		AAT CAGCGAC			:	1458
Wsuccinoge	:	GGC	ATGUAGUGAU			:	1446
		ggc	a cagcgac	tgggg			

Figure 2 - 45

Hsuis2BXA0	:	AACCCGGGCGGC	:	1421
Ghominis1	:		:	-
Ghominis21	:		:	-
Hfelis qb	:		:	~
Hbizzozero	:		:	-
Hbilis qb	:		:	-
Hsalomonis	:		:	-
Hpylori qb	:		:	-
Hcanis gb	:		:	-
Hcinaedilg	:		:	_
Hacinonych	:		:	-
Hnemestrin	:	A	:	1463
Hcholescys	:		:	-
Hpamatensi	:		:	-
Hmustelae!	:		:	-
Hrodentium	:		:	-
Hpullorum!	:		:	-
Hfennellia	:		:	-
Htrogontum	:		:	-
Hmuridarum	:		:	-
Hhepaticus	:		:	-
Abutzleril	:		:	-
Cjejunilgb	:		:	-
Wsuccinoge	:		:	-

Figure 2 - 46

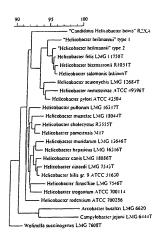


Fig 3A

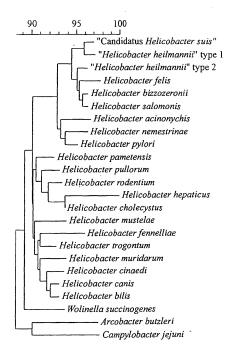


Fig 3B

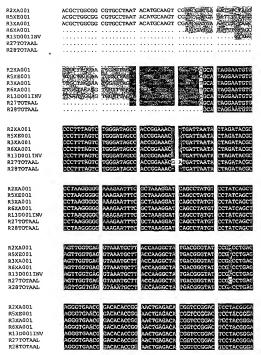


Figure 4 - 1

R2XA001 R5XE001 R3XA001 R6XA001 R13D001INV R27TOTAAL R28TOTAAL	SGCAGCAGTA GGGATATTG CTCAATGGGG GAAACCCTGA ACCAGCAACG SGCAGCAGTA GGGATATTG CTCAATGGGG GAAACCCTGA AGCAGCAACG SGCAGCAGTA GGGAATATTG CTCAATGGGG GAAACCCTGA AGCAGCAACG SGCAGCAGTA GGGAATATTG CTCAATGGGG GAAACCCTGA AGCAGCAACG GGCAGCAGTA GGGAATATTG CTCAATGGGG GAAACCCTGA AGCAGCAACG
R2XA001 R5XE001 R3XA001 R6XA001 R13D001INV R27TOTAAL R28TOTAAL	CCGCCTGGAC GATGAAGGTI CTAGGATTGT AAACTCCTTT TCTGAGAGAA CCGCGGGGAG GATGAAGGTI CTAGGATTGT AAACTCCTTT CCGCGGGGGAG GATGAAGGTI CTAGGATTGT AAACTCCTTT CCGGGTGGAG GATGAAGGTI CTAGGATTGT AAACTCCTTT CCGCGTGGAG GATGAAGGTI CTAGGATTGT AAACTCCTTT CCCCGTGGAG GATGAAGGTI CTAGGATTGT AAACTCCTTT CCCCGTGGAG GATGAAGGTI CTAGGATTGT AAACTCCTTTT CCTGAGGGAA CCCCGTGGAG GATGAAGGTI CTAGGATTGT AAACTCCTTTT CCTGAGGGAA CCCCGTGGAG GATGAAGGTI CTAGGATTGT AAACTCCTTTT
R2XA001 R5XE001 R3XA001 R6XA001 R13D001INV R27TOTAAL R28TOTAAL	GATAATGACG GTATCTCAGG AATAAGCACG GGCTAACTCC GTGCCAGGCA GATAAAGGACG GTATCTCAGG AATAAGCACG GGCTAACTCC GATAAGACGC GTATCTCAGG GATAAGACGC GTATCTCAGG GATAAGACGC GTATCTCAGG AATAAGCACG GGCTAACTC GATAATGACG GTATCTCAGG AATAAGCACG GGCTAACTC GATAATGACG GATAACTC GATACTCAGG GATAAGCACC GATAACTCC GATCCAGCA
R2XA001 R5XE001 R3XA001 R6XA001 R13D001INV R27TOTAAL R28TOTAAL	CCCCGTRAN ACCGAGGGTG CAASCGTRAC TCGGARTCAC TGGGCGTAAA CCGCGGTAAA ACCGAGGGTG CAASCGTRAC TCGGAARCAC TGGGCGTAAA CCGCGGGGGTG CAASCGTRAC TCGGAARCAC TGGGCGTAAA CCGCGGGGTGAA ACCGCGGGGTGAA ACCGCGGGGTGAA ACCGCGGGTGAA ACCGCGGGTGAA ACCGCGGTAAA ACCGCGGTAAA ACCGCGGGTAAA ACCGCGGGGTGAA ACCGCGGGGTAAA ACCGCGGGGTGAA ACCGCGGGGTAAA ACCGCGGGGTGAA ACCGCGGGGTAAA ACCGCGGGGTGAA ACCGCGGGGTAAA ACCGCGGGGTAAA TCGGAGGTGAA ACCGCGGGTAAA ACCGCGGGAAAA ACCGCGGGTAAA ACCGCGGGTAAA ACCGCGGGGTAAA ACCGCGGGTAAA ACCGCGGGGTAAA ACCGCGGGTAAA ACCGCGGGGTAAA ACCGCGGGGTAAA ACCGCGGGGTAAA ACCGCGGGGTAAA ACCGCGGGGTAAA ACCGCGGGGTAAA ACCGCGGGGTAAA ACCGCGGGGTAAA ACCGCGGGTAAA ACCGCGGGGTAAA ACCGCGGGGTAAA ACCGCGGGGTAAA ACCGCGGGGTAAA ACCGCGGGGTAAA ACCGCGGGGTAAA ACCGCGGGGTAAA ACCGCGGGGTAAA ACCGCGGGGTAAA ACCGCGGGGGTAAA ACCGCGGGGTAAA ACCGCGGGTAAA ACCGCGGGGTAAA ACCGCGGGTAAA ACCGCGGGGTAAA ACCGCGGGGTAAA ACCGCGGGGTAAA ACCGCGGGGTAAAA ACCGCGGGGTAAA ACCGCGGGGTAAAA ACCGCGGGGTAAAA ACCGCGGGGTAAAA ACCGGGGGTAAAAA ACCGCGGAAAAA ACCGCGGAAAAAAAAAA
R2XA001 R5XE001 R3XA001 R6XA001 R13D001INV R27TOTAAL R28TOTAAL	GAGCGTGTAG GCGGAATGAT AAGTCAGGCC TGAAATCCCC TGGCTTAAC- GAGCGTGTAG GCGGAATGAT AAGTCAGGCC TGAAATCCCC CGGCTTAAC- GAGCGTGTAG GCGGAATGAT AAGTCAGGCC TGAAATCCCC TGGCTTAAC- GAGCGTGTAG GCGGAATGAT AAGTCAGGCC GAAATCCCC TGGCTTAAC- GAGCGTGTAG GCGGAATGAT AAGTCAGGCC TGAAATCCCC TGGCTTAAC- GAGCGTGTAG GCGGAATGAT AAGTCAGGCC TGAAATCCCC TGGCTTAAC- GAGCGTGTAG GCGGAATGAT GAGTCAGGCC TGAAATCCCC TGGCTTAAC- GAGCGTGTAG GCGGAATGAT GAGTCAGGCC TGAAATCCCC TGGCTTAAC-
R2XA001 R5XE001 R3XA001 R6XA001 R13D001INV R27TOTAAL R28TOTAAL	CCGGACTCC GITTIGAAC ATCAITCING COCAACTCC GITTIGAAC ATCAITCING COCAACTC GITTIGAAC ATCAITCING COCAACTCC GITTIGAAC ATCAITCING COCAACTC GITTIGAAC ATCAITCING COCAACTC GITTIGAAC ATCAITCAITC COCAACTC COCAACTC COCAACTC COCAAC

Figure 4 - 2

R2XA001 R5XE001 R3XA001 R6XA001 R13D001INV R27TCTAAL R28TCTAAL	AACTCTTGGT AACTCTTGGT AACTCTTGGT AACTCTTGGT AACTCTTGGT AACTCTTGGT AACTCTTGGT	GTAGGGGT.A GTAGGGGT.A GTAGGGGTAA GTAGGGGTAA GTAGGGGTAA GTAGGGTAA GTAGGGGTAA	AATCCGTAGA AATCCGTAGA AATCCGTAGA AATCCGTAGA AATCCGTAGA AATCCGTAGA AATCCGTAGA	TATCAAGAAG TATCAAGAAG TATCAAGAAG TATCAAGAAG TATCAAGAAG TATCAAGAAG TATCAAGAAG	AATACTCATT AATACTCATT AATACTCATT AATACTCATT AATACTCATT AATACTCATT AATACTCATT AATACTCATT AATACTCATT
R2XA001 R5XE001 R3XA001 R6XA001 R13D0011NV R27TOTAAL R28TOTAAL	A-DORADDO A-DORADDO A-DORADDO A-DORADDO A-DORADDO A-DORADDO A-DORADDO	CCTGCTGAA CCTGCTGAA CCTGCTGGAA CCTGCTGGAA CCTGCTGGAA CCTGCTGGAA	CAT ACTGAC CAT ACTGAC CAT ACTGAC CAT ACTGAC CAT ACTGAC CATCACTGAC CATCACTGAC CATCACTGAC	CCTGATGCGC CCTGATGCGC GCTGATGCGC GCTGATGCGC GCTGATGCGC GCTGATGCGC GCTGATGCGC	GAAAGC TGC GAAAGC TGG GAAAGC TGG GAAAGC TGG GAAAGC TGG GAAAGC TGG GAAAGC TGG
R2XA001 R5XE001 R3XA001 R6XA001 R13D001INV R27TOTAAL R28TOTAAL	OKAGOR. DRAGOR. DRAGOR. DRAGORS DRAGOR. DRAGOR. DRAGOR. DRAGOR. DRAGOR. DRAGOR. DRAGOR. DRAGOR.	AGGATTAGAT AGGATTAGAT AGGATTAGAT TAGATTAGAT AGGATTAGAT AGGATTAGAT AGGATTAGAT	ACCCIGGTAG ACCCTGGTAG ACCCTGGTAG ACCCTGGTAG ACCCTGGTAG ACCCTGGTAG	TCCACGCCCT TCCACGCCCT TCCACGCCCT TCCACGCCCCT TCCACGCCCCT TCCACGCCCCT TCCACGCCCCT	AAACGATGGA AAACGATGGA AAACGATGGA AAACGATGGA AAACGATGGA AAACGATGGA AAACGATGGA
R2XA001 R5XE001 R3XA001 R6XA001 R13D001INV R27TOTAAL R2STOTAAL	TGCTAATTGT TGCTAATTGT TGCTAATTGT TGCTAATTGT TGCTAATTGT TGCTAATTGT TGCTAATTGT	CGGGGGGCTT CTCGGGGGCTT CTCGGGGGGCTT CGGGGGGCTT CTCGGGGGGCTT	GTCTCCTCGG GTCTCCTCGG GTCTCCTCGG GTCTCCTCGG GTCTCCTCGG GTCTCCTCGG	TAAT AGCT TAAT AGCT TAAT AGCT TAAT AGCT TAAT AGCT TAAT AGCT TAAT AGCT	AACGCATTAA AACGCATTAA AACGCATTAA AACGCATTAA AACGCATTAA AACGCATTAA AACGCATTAA
R2XA001 R5XE001 R3XA001 R6XA001 R13D001INV R27TOTAAL R28TOTAAL	G-ATCCCGCC G-ATCCCGCC G-ATCCCGCC G-ATCCCGCC G-ATCCCGCC G-ATCCCGCC	TGGGGAGTAC TGGGGAGTAC TGGGGAGTAC TGGGGAGTAC TGGGGAGTAC TGGGGAGTAC TGGGGAGTAC	GATEGCAAGA GATEGCAAGA GATEGCAAGA GATEGCAAGA GATEGCAAGA GATEGCAAGA GATEGCAAGA	TTAAAACTCA TTAAAACTCA TTAAAACTCA TTAAAACTCA TTAAAACTCA TTAAAACTCA TTAAAACTCA	AAGGAATAGA AAGGAATAGA AAGGAATAGA AAGGAATAGA AAGGAATAGA AAGGAATAGA AAGGAATAGA
R2KA001 R5KE001 R5KA001 R6KA001 R13D001INV R27TOTAAL R2STOTAAL	20000000000000000000000000000000000000	CACAAGCGGT CACAAGCGGT CACAAGCGGT CACAAGCGGT CACAAGCGGT CACAAGCGGT CACAAGCGGT	GGAGCATGTG GGAGCATGTG GGAGCATGTG GGAGCATGTG GGAGCATGTG GGAGCATGTG GGAGCATGTG	GTTTAATTCG GTTTAATTCG GTTTAATTCG GTTTAATTCG GTTTAATTCG GTTTAATTCG	AAGATACGCG AAGATACGCG AAGATACGCG AAGATACGCG AAGATACGCG AAGATACGCG
		Fig	ure 4 - 3		

R2XA001	AAGAACCTTA CCCAGGCTTG ACATTGATG AATCTACCC AAAAGGTGGA
	LAGAACCTTA CCCAGGCTTG ACATTGATG AATCTACCC AAAAGGTGGA
R5XE001	
R3XA001	AAGAACCTTA CCCAGGCTTG ACATTGATG AATCTACCC AAAAGGTGGA
R6XA001	AAGAACCTTA CCCAGGCTTG ACATTGATG AATCTACCCT AAAAGGTGGA
R13D001TNV	AAGAACCTTA CCCAGGCTTG ACATTGATG AATCTACCC AAAAGGTGGA
R27TOTAAL	AAGAACCTTA CCCAGGCTTG ACATTGATG AATCTACCC AAAAGGTGGA
R28TOTAAL	AAGAACCTTA CCCAGGCTTG ACATTGATGC AATCTACCC AAAAGGTGGA
R2XA001	GTGCCAGTTT ACTGGAGCET GAAAACAGGT GCTGCACGGC TGTCGTCAGC
R5XE001	GTGCCAGTTT ACTGGAGCAT GAAAACAGGT GCTGCACGGC TGTCGTCAGC
R3XA001	CTGCCAGTTT ACTGCAGC T GAAAACAGGT CCTGCACGGC TCTCGTCAGC
R6XA001	
R13D001INV	GTGCCAGTTT ACTGGAGGET GAAAACAGGT GCTGCACGGC TGTCGTCAGC
R27TOTAAL	GTGCCAGTTT ACTGCAGC"T GAAAACAGGT GCTGCAGGGC TGTCGTCAGC
R28TOTAAL	GTGCCAGTTT ACTGGAGCST GAAAACAGGT GCTGCACGGC TGTCGTCAGC
R2XA001	TCGTGTCGTG AGATGTTGGG TTAAGTCCCG CAACGAGCGC AACCCTCGTC
R5XE001	TOGRETOCITE AGATERITEGE PRARETCCCC CAACGAGCGC AACCGTCGTC
R3XA001	TCGTGTCGTC AGATGTTGGC TTAAGTCCCG CAACGAGCGC AACCCTCGTC
R6XA001	TOGTGTCGTG AGATGTTGGG PTAAGTCCCG CAACGAGCGC AACCCTCGTC
R13D001INV	TCGTGTCGTC AGATGTTGGG TTAAGTCCCC CAACGAGCGC AACCCTCGTC
R27TOTAAL	TOTTETEGTE AGATETIEGE TEAAGROCCE CAACGAGEGE AACCCTECTO
R28TOTAAL	TCGTGTCGTG AGATGTTGGG TTAACTCCCG CAACGAGCGC AACCCTCGTC
R2XA001	CTTAGFTGCC ATCAGTFCGG CTGGGGACTC TAAGGAGACT GCCTFCGTAA
R5XEO01	CTTAGTTGCC ATCAGTTCGG CTGGGCACTC TAAGGAGACT GCCTTCGTAA
R3XA001	CTTACTTCCC ATCACTTCCC CTCCCCACTC PAAGGAGACT CCCTTCCTAA
R6XA001	CTIVACTITICO ATCACTITICO CITOGGCACTO TAAGGAGACT GCCTTCGTAA
R13D001INV	CTTACTTGCC ATCACTTCGC CTCCCCACTC TAAGGACACT GCCTTCGTAA
R27TOTAAL	CTTAGTTGCC ATCAGTTCGC CTGGGCACTC TAAGGAGACT GCCTTCGTAA
R28TOTAAL	CTTAGTTGCC ATCAGTTCGG CTGGGCACTC TAAGGAGACT GCCTTCGTAP
R2XA001	GGAGGAGGAA GGCGAGGATG ACGTCAAGTC ATC.ATGGCC C.TTATGTC GGAGGAGGAA GGCGAGGATG ACGTCAAGTC ATC.ATGGCC C.TTATGACC
R5XE001	GGAGGAGGAA GGCGAGGATG ACCTGAAGTC ATC.ATGGCC C.TTA GCC
R3XA001	GGAGGAGGAA GGCGAGGATG ACGTCAAGTC ATC ATGGCC C TTA GCC
R6XA001	GGAGGAGGAA GGCGAGGATG ACGTCAAGTC ATC ATGGCC C.TTA GCC
R13D001INV	GGAGGAGGAA GGCGAGGATG ACGTCAAGTC ATCCATGGCC CCTTATGCCT
R27TOTAAL	GGAGGAGGAA GGCGAGGATG ACCTCAAGTC ATC.ATGGCC C.TTA GCC
R2STOTAAL	GGAGGAGGAA GGCGAGGATG ACGTCAAGTC ATC. ATGGCC C. TTA GCC
R2XA001	GGGGGTAGGG ACGTGGTAGA AWGGGATGTA CAAAGAGATG CAATGTGGTA
R5XEO01	GGGGCTACEC ACCTGCTACA ATGGGATGTA CAAAGAGATG CAATGTCGTA
R3XA001	ggggctac c acctgctaca atgggatgta caaagagatg caatgtcgta
R6XA001	GGGGCTACHC ACGTGCTACA ATGGGATGTA CAAAGAGATG CAATGTCGTA
R13D001INV	GGGGCTAC≅C ACGTGCTACA ATGGGATGTA CAAAGAGATG CAATGTCGTA
R27TOTAAL	GGGGCTACHO ACGTGCTACA ATGGGATGTA CAAAGAGATG CAATGTCGTA
R28TOTAAL	GGGGCTACMC ACGTGCTACA ATGGGATGTA CANAGAGATG CAATGTCGTA
WY O LO LANCE	CHARGACAGE WITH MICHOCATCHA CAMACACATE CHARGACATA

Figure 4 - 4

R2XA001	AGATGGAGCA	AAACTCAAAA	ACATOTOCCA	GTTCGGATTG	TGGTCTGCA
R5XE001	AGATGGAGCA	AAACTCAAAA	ATCTCCCA	GTTCGGATTG	TGGTCTGCA
R3XA001	AGATGGAGCA	AAACTCAAAA	ATCTCCCA	GTTCGGATTG	TGGTCTGCA
R6XA001	AGATGGAGCA	AAACTCAAAA	ATCTCCCA	GTTCGGATTG	TGGTCTGCA
R13D001INV	AGATGGAGCA	AAACTCAAAA	GGRTCTCCCA	GTTCGGATTG	TGGTCTGCA
R27TOTAAL	AGATGGAGCA	AAACTCAAAA	ATCTCCCA	GTTCGGATTG	TGGTCTGCA
R28TOTAAL	AGATGGAGCA	AAACTCAAAA	ATCTCCCA	GTTCGGATCG	TGGTCTGCA
R2XA001	CTCGACCACA		SHEEDING	XF6CF5FATE	accessoroses
R5XE001	CECGACCACA	Version of the Car	PATE CONTACTOR	ARCCICACUE	ACCENTATE
R3XA001	CTCGACCAC	W	STOCKE STOCKE	ATTENDED TO SECOND	MODE ATTEMEN
R6XA001	CTCGACCACA	NG TROATICA	2000	ATCENCASSIC	
R13D001TNV	CTEGACEACA			Sept.	VOSCAL ANSWER
R27TOTAAL	CTCCACCACA	News .	CHEMINA ANDRES	2620.	
R28TOTAAL	STEGASSACA	rve .			
R28TOTAAL	3146344334	BG			
R2XA001	EGGTGAATAC	GTTCCCGGGT	CTTGTACTCA	CCAATCAC	1335
R5XE001		GTTCCCGGGT	CTTGTACTCA	CCAA	1331
R3XA001	'₫G				1299
R6XA001	₫				1267
R13D001INV					1236
R27TOTAAL					1194
R28TOTAAL					1172

Figure 4 - 5

	1				50
2B%A001		ACGATGAAGC	CTAGCTTGCT	AGGTT	GTGGCGCACG
4AXA001		ACGATGAAGC		AGGTT	GTGGCGCACC
6W06001	10CANG ICOA				GTGGCGCACG
V14D001					GTGGCGCACG
V19DINV001					
ATADIMAGAT				<u>M</u>	GTGDHGCACG
					100
000-004	51	_		-	100
2BXA001	GGTGAGTAAT	GCATAGATGA	CATGCCCTTT	AGTTTGGAAT	AGCCÁCTAGA
4AXA001	GGTGAGTAAT	GCATAGATGA	CATGCCCTTT	AGTTTGGAAT	AGCCACTAGA
6W06001	GGTGAGTAAT	GCATAGATGA	CATGCCCTTT	AGTTTGGAAT	AGCCACTAGA
V14D001	GGTGAGTAAT	GCATAGATGA	CATGCCCTTT	AGTTTGGAAT	AGCCACTAGA
V19DINV001	GGTGAGTAAT	GCATAGATGA	CATGCCCTTT	AGTTTGGAAT	AGCCACTAGA
	101	-			150
2BXA001	A. ATGGTGAT	TAATACCAAA	TACTACCTTA	CGAGGGAAAG	ATT ATCCCT
4AXA001	A. ATGGTGAT	TAATACCAAA	TACTACCTTA	CGAGGGAAAG	ATT ATCGCT
6W06001	A. ATGGTGAT	TAATACCAAA	TACTACCTTA	CGAGGGAAAG	ATT ATCGCT
V14D001	ACATGGTGAT	TAATACCAAA	TACTACCTTA	CGAGGGAAAG	ATTOATCGCT
V19DINV001	DATECTGAT	TAATACCAAA	TACTACCTTA	CGAGGGVNAG	ATT ATCGCT
	151				200
2BXA001	ANAGGATTCC	TCTATCTCCT	ATCAGCTTGT	TGG . TGAGGT	AAAGGCTCAC
4AXA001	AAAGGATTGG	TOTATGTOCT	ATCAGCTTGT	Nee ive eer	AAAGGCTCAC
6W06001	AAAGGATTGG	TCTATGTCCT	ATCAGCTTGT	PGG. TGAGGE	AAAGGCTCAC
V14D001	AAAGGATTGG	TCTATGTCCT	ATCAGCTTGT	TGG TGAGGE	AAAGGCTCAC
V14D001	AAAGGATTGC				
ATABTMARAT	AMEGAMIGG	TCTATGTCCT	ATCAGCTTGT	TGCCTGAGGT	AAAGGCTCAC
	201				0.00
2010.001		Control of the Control	-	-	250
2BXA001	CAAGG CTAT	GACGGGTATC	CGGCCTGAGA	GGGTGAGCGG	ACACACTGGA
4AXA001	CAAGC.CTAT	GACGGGTATC	CGGCCTGAGA	GGGTGAGCGG	ACACACTGGA
6W06001	CAAGC CTAT	GACGGGTATC	CGGCCTGAGA	GGGTGAGCGG	ACACACTGGA
V14D001	CAAGG . CTAT	GACGGGTATC	CGGCCTGAGA	GGGTGAGCGG	ACACACTGGA
V19DINV001	CAAGGECTAT	GACGGGTATC	CGGCCTGAGA	GGKTGAGCGG	ACACACTGGA
	251			Secretar	300
2BXA001	ACTGAGACAC	GGTCCAGACT	CCTACGGGAG		GGAATATTGC
4AXA001	ACTGAGACAC	GGTCCAGACT	CCTACGGGAG	GCAGCAGTAG	GGAATATTGC
6W06001	ACTGAGACAC	GGTCCAGACT	CCTACGGGAG	GCAGCAGTAG	GGAATATTGC
V14D001	ACTGAGACAC	GGTCCAGACT	CCTACGGGAG	GCAGCAGTAG	GGAATATTGC
V19DINV001	ACTGAGAGAC	GGTCCAGACT	CCTACGGGAG	GCAGCAGTAG	GGAATATTGC
	301				350
2BXA001	TUAATGGGGG	AAACCCTGA	AGCAGCAACG	CCCCCTGGAC	CATGAAGGTO
4AXA001	TCAATGGGGG	AAACCCTGA	AGCAGCAACG	CCCCCTCGAC	GATGAAGGTT
6W06001	TCAATGGGGG	AAACCCTGA	AGCAGCAACG	CCGCGTGGAC	GATGAAGGTT
V14D001	TCAATGGGGG	AAACCCTGA	AGCAGCAACG		GATGAAGGTT
V19DINV001	TCAATGGGGG	GAAACCCTGA	AGCAGCAACG		GATGAAGGT
VISDIMVOOL	A GAVA TELEFORE	Garage	ALGORIGICAL ACTION	CCGCG-GGAG	GATGAAGGI.
	351				400
2BXA001	TTAGGATCGT	AAACTCCTTT	TGTTAGAGAA	CATAATGACG	GWWGWWWGG
4AXA001	TTAGGATCGT	AAACTCCTTT	TETTAGAGAA		
				GATAATGACG	GTATCTAACG
6W06001	TTAGGATCGT	AAACTCCTTT	TGTTAGAGAA	GATAATGACC	GTATCTAACG
V14D001	TTAGGATCGT	AAACTCCTTT	TGTTAGAGAA	CATAATGACG	GTATCTAACG
V19DINV001	TTAGGATCGK	AAACTCCTTT	TGTTAGAGAA	GATAATGACC	GTATCTAACG

Figure 5 - 1

		401				450
2BXAC	001	AATAAGCACC	GGCTAACTCC	CTGCCAGCAG	CCGCGGTAAC	ACGGAGGGTC
4AXAC	001	AATAAGCACC	GGCTAACTCC	GTGCCAGCAG	CCGCGGTAAT	ACGGAGGGTG
6W060	001	AATAAGCACC	GGCTAACTCC	GTGCCAGCAG	CCGCGGTAAT	ACGGAGGGTC
V14D0		AATAAGCACC	GGCTAACTCC	GTGCCAGCAG	CCGCGCTAAT	ACCGAGGGTC
V19DINV		AATAAGCACC	GGCTAACTCC	GTGCCAGCAG	CCGCGGTAAT	ACGGAGGGTC
VIJDINVO	,01	TOTAL MISICANCE	SGC 1AAC ICC	STOCCAGCAG	CCGCGG! AA!	ACGGAGGGTC
		451				500
2BXAC	101	CAACCGTTAC	TCGGAATCAC	20000000112	GAGTGCGTAG	GCGGGGAGGA
4 A X A C		CAAGCGTTAC	TEGGAATEAE	TGGGCGTAAA		
				TGGGCGTAA	GAGTGCGTAC	GCGGG AGGA
6W060		CAAGCGTTAC	TCGGAATCAC	TGGGCGTAAA	GAGTGCGTAG	GCGGG . AGGA
V14D0		CAAGCGTTAC	TEGGAATEAC	TGGGCGTAAA	GAGTGCGTAG	GCGGG . AGGA
V19DINV(001	CAAGCGTTAC	TCGGAATCAC	TGGGCGTAAA	GAGTGCGTAG	GCCGC . AGGA
		501	~			550
2BXA		CAAGTCAGGT	GTC AAATC	CTATEG. CTT	AACCATAGAA	CTGCATTIGA
4AXAC		CAAGTCAGGT	GTG AAATC	CTATEGECTI	AACCATAGAA	CTGCATTTGA
6₩060		CAAGTCAGGT	GTG AAATC	CTATOE CTT	AACCATAGAA	CTGCATTTGA
V14D0		CAAÇTCAGGT	GTG AAATC	CTATGG CTT	AACCATAGAA	CTGCATTTGA
V19DINV	001	CAAGTCAGGT	GTGTGAAATC	CTATGE CTT	AACCATAGAA	CTGCATTTBA
		551			-	600
2BXA	001	AACTATCCTT	CTGGAGIGTG	GGEGAGGTAC	GTGGAATTCT	TGGTGTAGGG
4AXA(001	AACTATECTT	CTGGAGTGTG	GG#GAGGTAG	GTGGAATTCT	TGGTGTAGGG
6W050	100	AACTATCCTT	CTGGAGTGTG	GGGGGGAG	GTGGAATTCT	TGGTGTAGGG
V14D0	001	AACTATCCTT	CTGGAGTGTG	GGEGAGGTAG	GTGGAATTCT	TGGTGTAGGG
V19DINV	001	AACTATCCTT	CTGGAGTGTG	GG GAGGTAG	GTGGAATTCT	TGGTGTAGGG
		601				650
2BXAC	001	CGTAAAATCC	GTAGAGATCA	AGAGGE ATAC	CONVERTE DEEP	AGGCGACCTG
4AXAC	001	GETAAAATCC	GTAGAGATCA	AGAGGEATAC	CATTE CGA	AGGCGACCTG
6W060	001	G. TAAAATCC	GTAGAGATCA	AGAGGEATAC	CATTO COA	AGGCGACCTG
V14D0	001	G. TARAATCC	GTAGAGATCA	AGAGGATAC	CATTG .CGA	AGGCGACCTG
V19DINV	001	C. TARANTCO	GTAGAGATCA	AGAGGGATAC	CATTCCCCA	AGGCGACCTG
		o-mercan	CALL THE TAXABLE	1000	A STATE OF THE PARTY OF THE PAR	nessee measure
		651				700
2BXA	001	CTGGAACATC	ACTGACGCTG	ATTGCACGAA	ACCEPTEGES.	AGEAAACAGG
4AXA		CTGGAACATC	ACTGACGCTG	ATTGCACGAA	AGCGTGGGGG	AGCAAACAGG
6W060		CTGGAACATE	ACTGACGCTG	ATTGCACGAA	AGCGTGGGG.	RGCAAACAGG
V14D		CTGGAACATC	ACTGACGCTG	ATTGCACGAA	ACCGTEGGE.	AGCAAACAGG
V19DINV		CTGGAACATC	ACTGACGCTG	ATTGCACGAA	ACCCTCCCC.	AGCAAACAGG
VIJDIN.		- CO		A. FOCACOADA	Mercer Contract	HGCHAMCAGG
		701				750
2BXA	001	MATERIAGENER	CCTGGTAGTC	CACGCCCTAA	ACCAT GOAT	
4AXA		GA PRAGATIAG	CCTGGTAGTC	CACGCCCTAA	ACCATHCCAT	GCTAGTTGTT
6W060		TAGATAC		CACGCCCTAG		GCTAGTTGTT
V14D			CCTGGTAGTC	CACGCCCTAA	RCGAVE . CGAVE	GCTAGTTGTT
		TTAGATAC	CCTGGTAGTC	CACGCCCTAA	ACGAT . GGAT	GCTAGTTGTT
V19DINV	OOL	- TEPAGATIAIC	CCTGGTAGTC	CACGCCCTAA	REGEVE . GGEVE	GCTAGTTGTT
		751				
2011		त्रा संस्कृतः संसम्बद्धाः	-	-	-	800
2BXA(TGTCTTTCCA	GTAATGCAGS	TA CGCCTTA	AGCATCCCGC
4AXA		GGGAAGGCTT	TGTCTTTCCA	GTAATGCAGC	TAMCGCCTTA	AGCATCCCGC
6W060		GGGA . GGCTT	TGTCTTTCCA.	GTAATGCAGC	TAL CGCCTTA	AGCATCCCGC
V14D0		GGGA. GGCTT	TGTCTTTCCA	GTAATGCANC	TACCCCTTA	AGCATCCCGC
V19DINV	001	GGGA GGCTE	TGTCTTTCC2	GTAATGCAGC	PARCECCTIVE	AGCATCCCGC

Figure 5 - 2

	801				050
20112.004			~	-	850
2BXA001	CTGGGGAGTA	CGGTCGCAAG	ATTAAAACTC	AAAGG . AATA	GACGGGGACC
4AXA001	CTGGGGAGTA	CGGTCGCAAG	ATTAAAACTC	AAAGG . AATA	GACGGGGACC
6W06001	CTGGGGAGTA	CGGTCGCAAG	ATTAAAACTC	AAAGG . AATA	GACGGGGACC
V14D001	CTGGGGAGTA	CGGTCGCAAG	ATTAAAACTC	AAAGG AATA	GACGGGGACC
V19DINV001	CTGGGGAGTA	CGGTCGCAAG	ATTAAAACTC	AAARQEAATA	GACGGGGACC
	851				900
2BXA001	EGCACAAGCC	GTGGAGCATC	FICETOTIANTI	CGANG TACA	CGAAGAACC.
4AXA001	CGCACAAGCG	GTGGAGCATG	TGGTTTAATT	CGACGATACA	CGAAGAACC.
				CGACCAIVACA	
6W06001	CGCACAAGCG	GTGGAGCATG	TGGTTTAATT	CGATGETACA	CGAAGAACC.
V14D001	CGCACAAGCG	GTGGAGCATG	TGGTTTAATT	CGAEGETACA	CGAAGAACC.
V19DINV001	CGCACAAGCG	GTGGAGCATC	TECTTTAATT	CGAGGWTACA	CGAAGAACC
	901				950
2BXA001	PTACCTAGGC	PTGACATTG	AAGGAATICC	C. PAGAAATA	GGGGAGTGTC
4AXA001	TTACCTAGGC	TTGACATTC	ANGGAATTCC	C. TAGAAATA	GGGGAGTGTC
6W06001	TTACCTAGGC	TTGACATTG	AAGGAATTCC	CETAGARATA	GGGGAGTGTC
V14D001	TTACCTAGGC	TTGACATTC	AAGGAATTCC	COTAGAAATA	GGGGAGTGTC
V19DINV001	TTACCTAGGC	CTTGACATTG	AAGGAATTCC	CETAGAAATA	
ATADIMACOT	TACCTAGGC	CITGACATTE	AMGGAATTICC	CONTRICTOR STATE	GGGGAGTGTC
	951				
					1000
2BXA001	TAGCTTGCTA	GACCCTGAAA	ACAGGTGCTG	CACGGCTGTC	GTCAGCTCGT
4AXA001	TAGCTTGCTA	GACCETGAAA	ACAGGTGCTG	CACGGCTGTC	GTCAGCTCGT
6W06001	TAGCTTGCTA	GACCCTGAAA	ACAGGTGCTG	CACGGCTGTC	GTCAGCTCGT
V14D001	TAGCTTGCTA	GACCCTGAAA	ACAGGTGCTC	CACGGCTGTC	GTCAGCTCGT
V19DINV001	PAGCTTGCTA	GACCCTGAJA	ACAGGTGCTG	CACGGCTGTC	GTCAGCTCGT
	1001				1050
2BXA001	GTCGTGAGAT	GTTGGGTTAA	GTCCCGCARC	GAGCGCAACC	C. PITTTTCT
4AXA001	GTCGTGAGAT	GTTGGGTTAA	GTCCCGCAAC	GAGCGCAACC	C. IVOVIVICIO
6W06001	GTCGTGAGAT	GTTGGGTTAA	GTCCCGCAAC	GAGCGCAACC	C. PROTECTO
V14D001	GTCGTGAGAT	GTTGGGTTAA	GTCCCGCAAC	GAGCGCAACC	
V19DINV001	GTCGTGAGAT	GTTGGGTTAL	GTCCCGCAAC	GAGCGCAACC	
VIJDINVOGI	SECOTORORI	OT TOOGT LAP	GICCCGC AMC	GAGCGCAACC	C. TETTTCTT
	1051				
2BXA001	SCTTCCTAAC	Account to the	000000000000		1100
4AXA001	ÄGTTGCTÄÄC	AGGTT	GCGCACTCTA	AGAAGACTGC	CTGCGTAAGC
		AGGTT	ĞČGCÄCTCTA	AGAAGACTGC	CTCCGTAAGC
6W06001	AGTTGETAAC	AGGTT	GCGCACTCTA	AGAAGACTGC	CTGEGTAAGC
V14D001	agttgctáac	AGGT: TATGT	GCGCACTCTA	AGAAGACTGC	CTGCGTAAGC
V19D1NV001	AGTTGCTAAC	AGGTT - T	GCGCACTCTA	AGAAGACTGC	CTGCGTAAGC
	1101				1150
2BXA001	AGGAGGAAGG	TGAGGACGAC	GTCAAGTCAT	CATGGCCCTT	ACCCCTAGGC
4AXA001	AGGAGGAAGG	TGAGGACGAC	GTCAAGTCAT	CATGGCCCTT	ACGCCTAGGG
6W06001	AGGAGGAAGG	TGAGGACGAC	GTCAAGTCAT	CATGGCCCTT	ACCCCTAGGG
V14D001	AGGAGGAAGG	TGAGGACGAC	GTCAAGTCAT	CATGGCCCTT	ACGCCTAGGC
V19DINV001	AGGAGGAAGE	TGAGGACGAC	GTCAAGTCAC	CATGGCCCTT	ACCCTAGGC
					MACINI PROCESS
	1151				1200
2BXA001	CONCACANCE	GCTACAATGC	GGTGCACAAA	GAGATGCAAA	GCCGCGAGGC
4AXA001	CTACACACGT	GCTACAATGG			
			GGTGCACAAA	GAGATGCAAA	GCCGCGAGGC
6W06001	CTACACACGI	GCTACAATGG	GGTGCACAAA	GAGATGCAAA	GCCGCGAGGC
V14D001	CTACACACGT	GCTACAATGG	GGTGCACAAA	GAGATGCAAA	GCCGCGAGGC
V19DINV001	CTACACACGT	GCTACAATGG	GGTGCACAAA	GAGATGCAAA	GCCGCGAGGC

Figure 5 - 3

	1201				1250	
2BXA001	AGAGCTAATC	TATAAAACAC	CTCCTAGTTC	GGATTGCAGG	CTGCAACTCG	
4AXA001	AGAGCTAATC	TATAAAACAC	CTCCTAGTTC	GGATTGCAGG	CTGCAACTCG	
6W06001	AGAGCTAATC	TATAAAACAC	CTCCTAGTTC	GGATTGCAGG	CTGCAACTCG	
V14D001	AGAGCTAATC	TATAAAACAC	CTCCTAGTTC	GGATTGCAGG	CTGCAACTCC	
V19DINV001	AGAGCTAATC	TATAAAACAC	CTCCTAGTTC	GGATTGCAGG	CTGCAACTCG	
	1251				1300	
2BXA001	CCTGCATGAA	GCTGGAAT . C	GCTAGTAA . T	CCCAAA TCA	CCTATCTTCC	
4AXA001		GCTGGAAT.C	GCTAGTAA.T	CGCAAA. TCA	SCTATGTTGC	
6W06001	CCTCCATGAA	GCTGGAAT .C	GCTÄGTÄA.T	CCCAAA TCA	CCTATCTTCC	
V14D001	CETGCATGAA	GCTGGAAT .C	GCTAGTAA.T	CCCAADATCA	CCTATGTTGC	
V19DINV001	CCTGCATGAA	GCTGGAAWTC	GCTAGTAAAT	CGCAÄA	GCTATGTTGC	
	1301				1350	•
2BXA001	GGTGAATA .C	GTTCCC GGG	TCTTGTACTC	ACCCCCC. CO	CACACC ATTE	
4AXA001		GTTCCC .CCC	CCTTCTACTC	ACCGCCC . GT	CACACC ATC	
6W06001		Grikaca eee	TCTTGTACTC	ACCCCCC. CO	CACACO ATC	
V14D001	SCITCHARM C	GETTOCOCCECE	TETTGTACTC	ACCGCCCCCT	CACACC ATG	
V19DINV001		GTKCCCCGGG	TCTTGTACTC	ACCGCCCCGT	CACACCCATG	
	1351				1400	
2BXA001		TTGCCTTAAG	TCAGGATGCT	AAAGCAGCTA	CTCCCCACCG	
4AXA001		TTGCCTTAAG	TCAGGATGCT	AAAGCAGCTA	CTGCCCACGG	
6W06001		TTGCCTTAAG	TCAGGATGCT	AAAGCAGCTA	CTGCCCACC.	
V14D001	GCAGTTGTGT	TTGCCTTAAG	TCAGGATGCT	AAAGCAGCTA	91/6909/06	
V19DINV001		TTGCCTTAAG	TCAGGATGCT	AAAGCAGCTA	CTGCCCACC.	
		7				
	1401	3 2/2			1447	
2BXA001			AAGTCGTAAC	AAGGTAACCC	GGGCGGC	1423
4AXA001	CACACACAGC	TGGGGTG				1400
6W06001		AQ				1353
V14D001	CACACACAGC	B				1355
V19DINV001	CACACACAGC					1358

Figure 5 - 4



EUROPEAN SEARCH REPORT

DOCUMENTS CONSIDERED TO BE RELEVANT

Application Number EP 99 87 0035

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X	helicobacter hepati sequence of its rRN JOURNAL OF CLINICAL	MICROBIOLOGY, 1995 (1995-05), pages 1982	1-10	
X,D	feces and descripti pametensis sp. nov. INTERNATIONAL JOURN	es from bird and swine on of Helicobacter (AL OF SYSTEMATIC (JUL) 44 (3) 553-60.,	1-10	TECHNICAL FIELDS SEARCHED C12Q
X	Sequence of region from HTLV-III, LAV XP002110984 * abstract *	.0072; 09 april 1991 of gp 160 glycoprotein of and ARV. HUTHWEST FOUND BIOMED EE (US))	1,5,6,10	
	The present search report has		L	
	Piece of search THE HAGUE	Date of completion of the assect 4 August 1999	Reu	ter, U
X : part Y : part doo A : tect O : nor	ATEGORY OF CITED DOCUMENTS society relivant if taken alone society relivant if combined with ano ument of the same category innological background entitler disclosure mediate document	T : theory or principle E : earlier patent dos after the filing dat	e underlying the current, but public in the application or other reasons	invention shed on, or

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